



Review Article

Comprehensive review of *Tilia* L.: phytochemical profiles, edible value, therapeutic potentials, and ecological significance

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Received: 24 April 2024 / Revised: 3 July 2024 / Accepted: 4 July 2024

Abstract: The genus *Tilia* belongs to the Malvaceae family. There are approximately 400 species. The native range of this genus is Temp, Northern Hemisphere to Mexico. The Malvaceae family is a large family in plant classification and includes 245 accepted genera, of which the genus *Tilia* is one. Phylogenetic relationships and genetic variation of the genus were studied using simple sequence repeat (SSR) markers, microsatellite markers, and Illumina sequencing techniques. *Tilia* L. has an important economic value. Flavonoids, terpenoids, phenols, organic acids, and other metabolites have been isolated and extracted from the flowers, shoots, leaves, and bracts of different species of *Tilia* L., and phytochemical studies have shown that these biologically active components can be anti-inflammatory, analgesic, anticancer, anti-anxiety, depressive, and antioxidant and have a protective effect against nerve damage. *Tilia* L. flowers are fragrant and are a good source of honey plants. As one of the world's five main street trees, on the lightening heavy metal adsorption, *Tilia* L. plays an important role in environmental pollution. Studies on landscaping, urban environments, and arboreal applications comprehensively highlight the ecological significance of the species. A fraction of the species in the genus *Tilia* is on the International Union for Conservation of Nature and Natural Resources (IUCN) endangered list and requires immediate attention. This review will synthesize the research progress on the genus *Tilia* from multiple perspectives, including a brief overview of *Tilia* L., analysis of its genetic and phylogenetic relationships, exploration of its edible and medicinal value, examination of the pharmacological actions of isolated metabolites, and considerations for its ecological protection and conservation.

Keywords: *Tilia* L.; phylogenetic relationships; edible value; isolated metabolites; pharmacology; ecological functions

Citation: Zhou Y. J., Ren Q., Shen Y. B. Comprehensive review of *Tilia* L.: phytochemical profiles, edible value, therapeutic potentials, and ecological significance. *Food & Medicine Homology*, 2025, 2: 9420035. <https://doi.org/10.26599/FMH.2025.9420035>

1 Introduction

Tilia L., commonly known as linden or basswood, encompasses a group of deciduous trees renowned for their heart-shaped leaves and fragrant flowers. These trees are prevalent in temperate regions across the Northern Hemisphere, including North America, Europe, and parts of Asia^[1]. *Tilia* L. is classified under the family Malvaceae according to *The Plant List* (2023)^[2], *Tilia* L. comprises approximately 423 species, with 46 recognized species names. Additionally, data from World Flora Online indicate that *Tilia* species range from 23 to 40, including 15 endemics^[3]. *Tilia* L. holds vast potential for various applications. Currently, a smaller portion of research by domestic and international scholars focuses on its physiological and molecular biological characteristics, while most studies are concentrated on its economic, medicinal, ecological, and cultural functions. *Tilia* L. is a crucial source of nectar for honey production, and its wood is used for furniture and carving. The interaction between its roots and soil

microorganisms can yield valuable truffles, and linden logs can produce shiitake mushrooms. Extracts from *Tilia* L. possess medicinal properties, including antidepressant and anticancer effects. Linden flower tea has a long history of consumption in Europe and is a traditional medicinal plant for many cultures. In Europe and America, *Tilia* L. is extensively used as a street tree, with strong capabilities to absorb pollutants and heavy metals, thus purifying the air and regulating the ecosystem. Despite its wide distribution in temperate forests globally, some species are endangered due to deforestation and the difficulty of seed propagation, necessitating conservation efforts. Although *Tilia* L. is of significant importance, research on this genus remains fragmented. Currently, no comprehensive review of *Tilia* L. exists. Recent years have seen growing interest in the economic, medicinal, and ecological benefits of *Tilia* L. This review is crucial for advancing the development and utilization of food and medicinal products derived from *Tilia* L. By consolidating current research, this review seeks to identify knowledge gaps and provide

a foundation for future studies and potential commercial exploitation of these valuable trees.

2 Survey methodology

A meticulous review of literature was undertaken by examining various databases, including PubMed, Web of Science, LISTA, Google Scholar, and CNKI. Utilized descriptors, in diverse combinations, encompassed: ‘*Tilia*’, ‘*Tilia* economic’, ‘*Tilia* taxonomy’, and ‘*Tilia* metabolites’. Furthermore, investigations into linden plants entailed extracting pertinent data from leading plant databases, notably the Kew Plant Database, the Red List of Rare and Endangered Plants, and the International Plant Names Index. This study synthesizes insights from our group’s prior research on the endemic *Tilia miqueliana* Maxim., native to Eastern China. A thorough evaluation of relevant literature was conducted, emphasizing key references integral to the study’s themes. These references formed the basis for the tables presented herein. Complementing this, a manual search was executed to uncover additional relevant studies. Exclusions from this analysis were studies with unreliable data extraction, those presenting only abstracts without full-text access, and literature comprising books and conference papers.

3 Overview of *Tilia* L.

Tilia L. (Fig. 1F), a valuable and robust plant species, reaches up to 20 m in height and features gray bark with spherical fruit. This genus is characterized by deciduousness, alternating leaves, axillary inflorescences, and caducous stipules. The leaf blades are often oblique at the base, varying from cordate to truncate or rounded (Figs. 1A, 1B). Leaf margins are typically serrated, although some may be smooth, and hairy domatia are common in vein axils. The

bracts (Fig. 1C), notable for their band-like shape and size, adhere to the flower peduncle and are persistent. *Tilia* L. flowers (Figs. 1D, 1E) are bisexual and exhibit five sepals with an adaxial nectary at the base, contributing to its reputation as an excellent honey-producing species. The flowers, blooming from May to June, are fragrant, with five petals arranged imbricately. Fruit shapes vary from globose to obovoid, ellipsoid, or ovoid, with a hairy pericarp that is either woody or fragile and remains closed at maturity. Occasionally, the pericarp is leathery and splits when dry^[4]. Several species that are significant for their distinctive characteristics and extensive applications. *Tilia americana* (American basswood), native to eastern North America, can grow up to 40 m tall and is recognized for its large leaves and fragrant flowers. It is highly valued for wood carving, furniture making, and honey production. *Tilia cordata* (small-leaved linden), native to Europe, typically reaches heights of up to 30 m and features small, heart-shaped leaves. It is commonly used in urban landscaping, honey production, and traditional medicine. *Tilia platyphyllos* (large-leaved linden) is widespread across Europe. It is distinguished by its larger leaves and adaptability to upland habitats. *Tilia × europaea* (common lime or European linden), a hybrid of *T. cordata* and *T. platyphyllos*, is widely planted in Europe for ornamental purposes^[5,6]. The *T. miqueliana* Maxim., native to the Nanjing area in Jiangsu Province, China, holds significant regional cultural significance and is renowned for its longevity. During the 2022 Nanjing Golden Tree King competition, a venerable specimen over 1,000 years old was discovered. This species offers multifaceted values, encompassing landscaping, nectar production, superior wood quality, Buddhist cultural significance, and pharmacological properties. The wood of *T. miqueliana* Maxim. is notable for its white, soft nature, dense and straight grain, silky luster, and aesthetic appeal. Its flexibility,

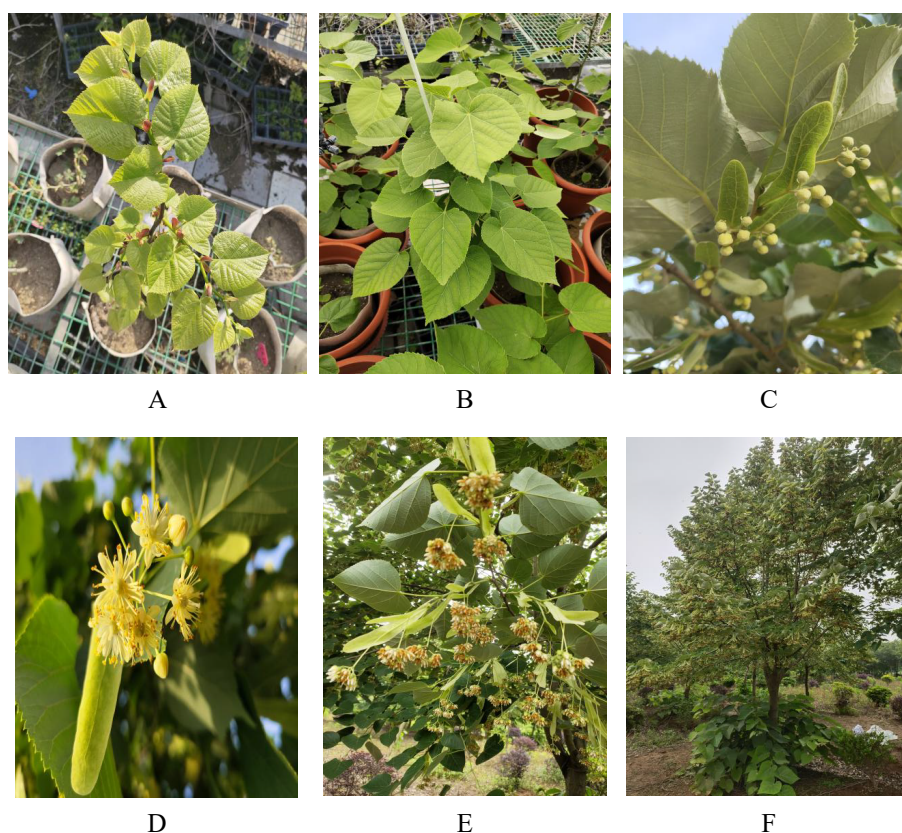


Figure 1 (A) Tender leaf, (B) Seedling, (C) Bracts and bud, (D) *T. cordata* flower, (E) *T. miqueliana* Maxim. flower, (F) Mature tree.

resistance to cracking, ease of processing, and excellent staining qualities make it ideal for construction, furniture, papermaking, carving, joinery, and other applications. Its odorless nature suits it for kitchen utensils such as cutting boards, barrels, and steamers. The species also possesses valuable bast fibers, known as “linden hemp,” with a hemp rate of 39.6%, suitable for producing rayon, rope, and textiles. Medicinally, the flowers and bark of *T. miqueliana* Maxim. are utilized, reflecting its deep roots in Buddhist culture. It is often revered as the “Bodhi tree” in certain locales, commonly planted around temples and monasteries, with its seeds frequently used in crafting Buddhist beads. The functions of each part of *Tilia* L. are shown in Fig 2.

The distinctive bracts of *Tilia* L., which are attached to the

stems of flower clusters, distinguish it from other taxa. However, species differentiation within the *Tilia* genus is challenging due to extensive hybridization, polyploidy, and subtle morphological differences. In the NCBI database, the genus *Tilia* is classified into the following species, subspecies and varieties: *T. americana* (American linden), variety *T. americana* var. *mexicana*, *T. americana* var. *neglecta*, and the hybrid *T. americana* × *Tilia* × *moltkei*. *T. amurensis*, *Tilia begoniifolia*, *Tilia caroliniana*, *T. caroliniana* subsp. *Heterophylla*, *Tilia chinensis*, *Tilia chingiana*, *T. cordata*, *T. cordata* subsp. *Cordata*, *T. cordata* subsp. *Sibirica*, *Tilia corylifolia*, *Tilia dasystyla*, *Tilia endochrysea*, *Tilia henryana*, *T. henryana* var. *Subglabra*, *Tilia hupehensis*, *Tilia hyrcana*, *Tilia japonica*, *T. japonica* var. *Japonica*, *Tilia kiusiana*, *Tilia koreana*,

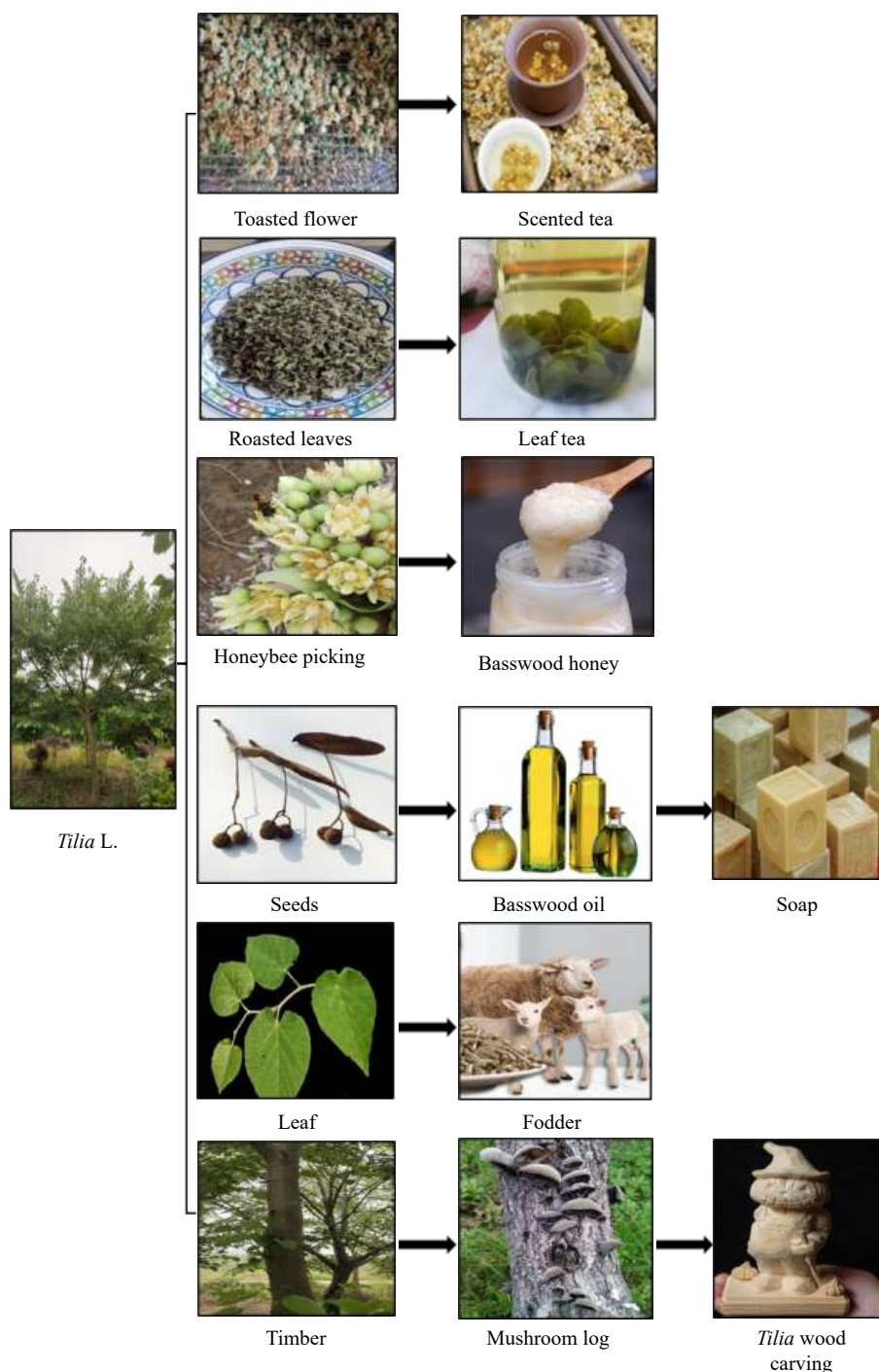


Figure 2 Utilization of several components of *Tilia* L.

Tilia mandshurica, *Tilia maximowicziana*, *Tilia megaphylla*, *T. miqueliana*, *Tilia mongolica*, *Tilia nasczokinii*, *Tilia nobilis*, *Tilia oliveri*, *Tilia paucicostata*, *T. paucicostata* var. *Dictyoneura*, *T. platyphyllos*, *Tilia rufa*, *Tilia taishanensis*, *Tilia taquetii*, *Tilia tomentosa*, *Tilia tuan*, *Tilia* × *euchlora*, *Tilia* × *europaea*, *Tilia* × *flaccida*, *Tilia* × *moltkei*, unclassified *Tilia*^[7]. In China, the *Tilia* genus comprises a diverse array of species, including *T. amurensis*, *T. breviradiata*, *T. callidonta*, *T. chenmoui*, *T. chinensis*, *T. endochrysea*, *T. henryana*, *T. hupehensis*, *T. integerrima*, *T. intonsa*, *T. japonica*, *T. kueichouensis*, *T. laetevirens*, *T. lepidota*, *T. likiangensis*, *T. mandshurica*, *T. membranacea*, *T. mesembrinos*, *T. miqueliana*, *T. mofungensis*, *T. mongolica*, *T. nanchuanensis*, *T. nobilis*, *T. oblongifolia*, *T. obscura*, *T. oliveri*, *T. omeiensis*, *T. paucicostata*, *T. populifolia*, *T. tristis*, *T. tuan*, and *T. yunnanensis*^[8].

4 Genetic and phylogenetic insights

Tilia L., as an angiosperm, possesses a large genome. Currently, the whole genome sequencing of the *Tilia* L. has not yet been completed, only partial studies on the chloroplast and plastid genomes of the *Tilia* L. have been conducted. The chloroplast genomes of *Tilia* L., despite their small size, play a crucial role in molecular systematics and phylogenetic analysis due to the predominant matrilineal inheritance in angiosperms. Zheng *et al.*^[9] elucidated the complete chloroplast genome of *T. mongolica* Maxim, revealing its close phylogenetic relationship with *T. taishanensis*. Furthermore, *T. endochrysea*, endemic to the southern boundary of the Chinese subtropical zone and distinguished by its dehiscent fruit, is posited as the basal taxon in the genus. This assertion is supported by its close affiliation with *Craigia yunnanensis* in phylogenetic analyses^[10,11]. Significant advancements were also made in the sequencing of the chloroplast genome of *T. taishanensis*, an endangered species endemic to China, using the Illumina HiSeq 2000 platform^[12]. This study confirmed the species' phylogenetic position and quadruple structure, consistent with other *Tilia* plants. Yan *et al.*^[13] conducted an extensive comparison of chloroplast genomes across five *Tilia* species, leading to the discovery of significant sequence repeats. Their analysis underscored the monophyly of all Malvaceae subfamilies. Yang *et al.*^[14] provided the first comprehensive chloroplast genome sequencing of *Tilia insularis*, native to Ulleung Island, Korea, comprising 131 genes with an overall guanine-cytosine content of 36.5%. This data contributed to understanding the phylogenetic relationships within the Malvaceae family, particularly in the Tilioideae subfamily. Illumina sequencing technology facilitated a comprehensive plastid genome sequencing, reaffirming its efficacy in phylogenetic analyses within *Tilia*. Cai *et al.*^[15] reported on the plastid genomes of four *Tilia* species, highlighting their consistency with the general angiosperm structure and similarity to other Malvaceae genomes. The low sequence divergence among these genomes is a trait common in long-lived tree genera. Additionally, to explore genetic variation within *Tilia*, we developed SSR and microsatellite markers, particularly focusing on *T. platyphyllos* and its relationship with *T. cordata*. These markers have proven invaluable in phylogeographical studies and in understanding hybridization patterns within the genus^[16]. Lastly, comparative transcriptional analyses by Kang *et al.*^[17] on *T. amurensis* during somatic embryogenesis identified 1,505 differentially expressed genes, including those related to auxin, developmental regulation, and signal transduction. Lobo *et al.*^[18] explored population

genetics and spring phenology of *T. cordata* in Denmark, identifying divergent selection and genetic drift as key factors. Evans and Morris^[19] analyzed population genetic structure of *T. americana* var. *caroliniana* using nuclear microsatellite loci, contributing to our understanding of genetic patterns in its US distribution. Notably, despite these findings, the genus lacks comprehensive studies on linden variant loci and taxon delimitation due to the insufficient informative sites from conventional genetic markers. Overall, research at the genetic level of the *Tilia* L. remains relatively limited. Existing studies primarily focus on utilizing various technological approaches to investigate its phylogenetic relationships and genetic variation. These efforts are of significant importance for the classification of *Tilia* L. populations and the identification of different species and subspecies.

5 Edible and medicinal uses of *Tilia* L.

Various parts of *Tilia* L. are utilized for their edible properties, offering diverse culinary applications. Linden leaves, characterized by their fine fiber texture and tender mouthfeel, are free from bitterness and highly palatable. They and young shoots are rich in polysaccharides and can be consumed raw or blanched in cold dishes. Additionally, due to their high antioxidant and flavonoid content, they are ideal for vegetable salads. In northern China, particularly in the Shanxi region, mature linden leaves are used to wrap sticky dough cakes and meat pies, known as "linden leaf cakes." This traditional practice mirrors the cultural significance of wrapping Zongzi, a rice pudding, in various leaves, including those from *T. tuan*, which also provide preservative and medicinal benefits^[20].

Linden flowers are widely used to make floral tea, valued for its calming and sleep-inducing properties. This tea can also relieve symptoms of colds, coughs, and sore throats, attributed to the beneficial compounds in linden flowers such as flavonoids, saponins, and tannins. Linden seeds, although not suitable for long-term storage, can be processed into a chocolate substitute or roasted to make a coffee-like beverage. Furthermore, *Tilia* L. roots form symbiotic relationships with truffles, producing unique subterranean fruiting bodies that hold significant economic value due to their rarity^[21].

The most notable edible product from *Tilia* L. is its honey, often referred to as "snow honey" due to its purity and whiteness. Although research on the secretion of linden flower nectar and the composition of linden honey is limited, existing studies highlight its quality. Sun *et al.*^[22] found that *Tilia amurensis* nectar secretion peaks midday, with an average yield of 8.58 mg per flower over a flowering duration of 6–8 days. Studies have also identified specific markers and compounds unique to *Tilia* L. honey. Labsvards *et al.*^[23] and Zielinski *et al.*^[24] used advanced analytical techniques to differentiate *Tilia* honey from multifloral types and identified unique markers like chenodeoxycholic acid derivatives and 4-(1-hydroxy-1-methylethyl) cyclohexane-1, 3-dicarboxylic acid. Moreover, Qiao *et al.*^[25] found compounds like methyl syringate and lindenin in *Tilia* honey, which contribute to its distinct characteristics.

Tilia L. offers significant edible and medicinal benefits through its leaves, flowers, seeds, and honey. The various bioactive compounds present in these parts underscore their potential for culinary and therapeutic applications. However, existing literature indicates that research on the edible value of *Tilia* L. is not yet comprehensive, suggesting substantial potential for further

development and application. Future studies could deepen our understanding of these properties, enhancing the utilization of *Tilia* L. in food and medicine.

6 Isolated metabolites and phytochemistry

The secondary metabolites of *Tilia* L. are highly abundant and can be extracted from various parts of the plant, including flowers, leaves, buds, and trunk. Extensive research has been conducted to isolate and identify these metabolites. For instance, using high-performance liquid chromatography, researchers have investigated the polarities of catabolites in cold extracts of senescent leaves of *T. cordata*. Scherl *et al.*^[26] identified two colorless and non-fluorescent chlorophyll catabolites, along with a yellow polar chlorophyll catabolite. Additionally, studies on the bark extract of *T. amurensis* identified lignan glycosides, fatty acids, flavan-3-ol, and coumarins^[27], while further analysis using HPLC extracted flavonoids and terpenoids, validating compounds such as epicatechin, nudiposide, lyoniside, and scopoletin, among others^[28,29].

Researchers have also examined the chemical composition of compounds in nutlets of *Tilia* L. Siger *et al.*^[30] analyzed carotenoids, phytosterols, fatty acids, and tocochromanols, identifying linoleic, oleic, and palmitic acids as predominant fatty acids. Linden seed oil exhibited high levels of phytosterols, with β -sitosterol being the most prevalent, and significant amounts of tocopherols and tocotrienols, about 93%. From the inflorescences of *T. tomentosa*, Frezza *et al.*^[31] isolated thirteen compounds, including oleanolic acid, shikimic acid, and quercetin-3-O-glucoside, with flavonoids, organic acids, and pentacyclic triterpenes being the major classes of these compounds. Seasonal changes in metabolites of *T. platyphyllos* bracts were studied using liquid chromatography electrospray ionization mass spectrometry (LC-ESI-MS) and data mining techniques, revealing high levels of polyphenolic compounds, flavonol glycosides, and catechins in younger tissues^[32].

The potential medicinal and ecological applications of *Tilia* L. are underscored by various studies. For instance, Milewska-Hendel *et al.*^[33] examined prenilylids, sodium, and chlorine levels in the leaves of *Tilia* $\times$ *euchlora*, assessing their role in defense against salt-induced stress. Ieri *et al.*^[34] characterized phytochemicals in *T. tomentosa* bud extracts, identifying key flavonols such as quercetin and kaempferol. Additionally, Symma *et al.*^[35] isolated six alkaloid compounds from dried inflorescences of different *Tilia* species, revealing that these alkaloids often possess dihydropyrrole and piperidine substructures. Traditional uses of *Tilia* L., such as treating influenza and psychological stress, have also been validated by modern studies. Selvi^[36] found increased phenolic and flavonoid content in infrared-dried leaves of *T. platyphyllos* Scop., while Pieczykolan *et al.*^[37] developed advanced methods to measure and isolate tiliroside from *Tilia* L. flowers. These findings emphasize the importance of accurately characterizing *Tilia* L. metabolites for advancing pharmacological research and therapeutic applications. Table 1 provides a summary of the natural chemical compounds extracted from various *Tilia* species and their corresponding pharmacological effects.

7 Pharmacology of *Tilia* L.

7.1 Traditional and contemporary therapeutic uses

Tilia species, have a rich history of use in traditional medicine

across various cultures, primarily for treating infections, anxiety, and other ailments. These plants are renowned for their pharmacological properties affecting the central nervous system. For instance, the hexane extract from *T. americana* var. *mexicana* has demonstrated depressant effects on the central nervous system, as reported by Aguirre-Hernandez *et al.*^[38]. Additionally, compounds from *T. amurensis* have shown significant neuroprotective effects against glutamate-induced neurotoxicity. In Korea, China, and Japan, *T. amurensis* is traditionally esteemed for its antitumor and anti-inflammatory properties^[39].

Globally, the genus *Tilia* is recognized for its therapeutic qualities, often consumed as tea for its analgesic, anticonvulsant, and tranquilizing effects. Various *Tilia* species play integral roles in traditional medicine, attributed to their inherent therapeutic properties. A study conducted in southwestern Lithuanian villages revealed the prevalent use of *T. cordata* for treating digestive and respiratory ailments^[40]. This species holds significant importance in traditional Lithuanian ethnobotany, a discipline that blends ancient customs with modern healing practices. The tradition of self-medication with homemade natural remedies remains widespread in Lithuania^[41]. In Estonia, over 50% of the usage of *Tilia* plants is dedicated to the preparation of recreational and medicinal teas, especially for treating colds in children^[42]. Similarly, in Alasehir, Turkey, *Tilia argentea* Desf. ex DC. is a predominant medicinal species, primarily associated with health maintenance and disease prevention^[43]. *Tilia* species are globally recognized for their extensive therapeutic applications in traditional medicine. Their central nervous system pharmacological properties make them valuable for treating a variety of conditions, from anxiety and infections to neuroprotection and anti-inflammatory needs. The continued use of *Tilia* in various cultural contexts underscores its enduring relevance and potential for future medicinal applications.

7.2 Antiviral properties

Kwon *et al.*^[44] conducted a study investigating the antiviral effects of *T. amurensis* honey against the influenza A virus in murine macrophages. Their findings indicate that this honey modulates the innate immune response, suggesting potential therapeutic strategies for treating influenza A. This research not only highlights the medicinal properties of *T. amurensis* honey but also underscores its economic value, given its enhanced applicability in antiviral treatments. In a complementary study, Marrassini *et al.*^[45] examined the traditional use of *Tilia* $\times$ *viridis* in Europe and the United States for alleviating anxiety and treating respiratory illnesses. Their investigation focused on the phytochemical properties of the ethanol extract, particularly its flavonoid content. The study demonstrated that the extract has significant antiproliferative effects on lymphoma cells, coupled with notable antioxidant capabilities. These properties contribute to the therapeutic potential of *Tilia* $\times$ *viridis*, reinforcing its use in traditional medicine. Both studies underscore the multifaceted medicinal benefits of *Tilia* L. products. The antiviral properties of *T. amurensis* honey and the therapeutic effects of *Tilia* $\times$ *viridis* extracts highlight their potential applications in modern medicine.

7.3 Cytotoxic Activity

Kim *et al.*^[46] conducted a comprehensive evaluation of the anticancer properties of lignan derivatives derived from *T. amurensis* Rupr. (Tiliaceae). Their study focused on the methanolic extract of the plant's trunk, which contained novel

Table 1 Natural product chemicals, used parts, curative effects, and extracts of different species of *Tilia* L.

Name of the species	Natural product chemicals	Used parts	Curative effects	Extracts	References
<i>T. platyphyllos</i>	Phytosterols, carotenoids, tocochromanols and fatty acid, squalene, vitamin E, flavonoid glycosides, catechins, procyanidins, quinic acid derivatives (including chlorogenic acid) and coumarins Protocatechuic acid, epicatechin	Seeds, bracts, flowers	Therapeutically useful		[30, 32]
<i>T. platyphyllos</i> Scop	phenolic acid and flavonoid, phenolic compounds		Antioxidant, anti-inflammatory and antitumor properties	Hydroethanolic extract	[52, 75]
<i>T. amurensis</i>	Coumarins, flavan-3-ol, fatty acid, lignan glycosides, flavonoids, terpenoids, epicatechin, nudiposide, lyoniside, and scopoletin	Barks	Antitumor, anti-inflammatory, neuroprotective activities against glutamate-injured neurotoxicity	EtOAc and CH ₂ Cl ₂ extract	[27, 29]
<i>T. amurensis</i> Rupr	Lignan derivatives, lignan glycosides, Isoflavonoid glycoside	Trunks	Anticancer, cytotoxicity against lung carcinoma, antiproliferative activities	Methanolic extract	[50]
<i>T. americana</i>	Flavonoid, tiliroside, rutin, quercitrin, quercetin glucoside, and kaempferol		Hypoglycemic activity, antioxidant activity, anxiolytic, neuroprotective effects Neuropharmacological activity, anxiolytic-like response, Antinociceptive activity, antidepressant activity, antioxidant, anticonvulsant activity; medicinal properties on the central nervous system, neuroprotective activity, hepatoprotective effects	Methanolic extract, aqueous and organic extract	[55, 68, 71, 72]
<i>T. americana</i> var. <i>mexicana</i>	Flavonoids, quercetin kaempferol glycosides, rutin, and isoquercitrin	Inflorescences, bracts, and leaves	Antioxidant, anticonvulsant activity; medicinal properties on the central nervous system, neuroprotective activity, hepatoprotective effects	<i>Tilia</i> inflorescences extracts hexane, organic extracts, methanol and aqueous extracts (AE)	[59, 61-63, 71, 72, 74]
<i>T. americana</i> var. <i>mexicana</i> (Schltdl) Hardin	Tiliroside, glucoside of quercetin, quercitrin, rutin, kaempferol	Bracts and flowers	Anxiolytic activity, treat nervous disorders, as sedative and to treat insomnia	Organic fraction extracts	[66]
<i>T. tomentosa</i>	Flavonols (quercetin, kaempferol, apigenin derivatives), nucleosides, phenolic acids, glycosylated flavonoids, oleanolic acid, maslinic acid, luteolin, rutin, tiliroside, ellagic acid, shikimic acid, and quinic acid	Buds, flowers, and bracts	Antioxidant	Bud extract	[31, 34, 53]
<i>T. tomentosa</i> Moench	Flavonols, particularly quercetin, kaempferol derivatives, and pectin	Buds, flowers	Effective sedative and anxiolytic compound, anti-spasmodic; antioxidant capacity, anxiolytic activity	Bud extract, flower extract	[54, 60, 65, 67, 77]
<i>T. kiusiana</i>	Lanostane-type triterpenoid, cholestane-type sterols		Cytotoxicity against two human cancer cell lines		[47]
<i>T. taquetii</i> Schneider	Phytol, isoquercitrin, oleanderolide, arjunolic acid, and maslinic acid Colorless nonfluorescent chlorophyll catabolites, polar yellow chlorophyll catabolite, flavan-3-ol derivatives, procyanidins and epicatechin	Leaves	Anti-wrinkle properties	Ethanol extract	[28]
<i>T. cordata</i>	Flavonoid glycosides, isoquercitrin, quercetin 3-O-glucoside-7-O-rhamnoside, and kaempferol 3-O-glucoside-7-O-rhamnoside	Senescent leaves, flowers	Colds, cough, fever, anti-inflammatory activity, pharyngitis, and tonsillitis	MeOH extract	[26, 76]
<i>Tilia petiolaris</i> DC		Inflorescences	Neuroactive	Ethanol extract	[70]
<i>Tilia</i> × <i>euchlora</i>	Prenyl lipids, sodium, and chlorine	Leaves	Defense salt stress		[33]
<i>Tilia</i> × <i>viridis</i>	Flavonoids, quercetin, kaempferol, glycosides, tiliroside, and rutin	Flowers	Treat anxiety, colds, bronchitis, fever, inflammations, and influenza; antiproliferative action on tumoral cells; free radical scavenging activity; antioxidant activity; macrophage activation; protective effect of apoptosis	Ethanol extract, aqueous and a dichloromethane extract	[45, 48]

lignan glycosides. These glycosides demonstrated significant cytotoxic effects against various cancer cell lines, highlighting their potential as effective anticancer agents. In a similar vein, Shimada *et al.*^[47] explored the anticancer efficacy of compounds isolated from the leaves of *T. kiusiana*. Their research identified a range of bioactive substances, including kiusianins, lanostane-type

triterpenoids, and cholestane-type sterols. These compounds exhibited notable cytotoxic activity against human cancer cell lines, further underscoring the potential of *Tilia* species in cancer treatment. These findings highlight the importance of further exploring the pharmacological properties of *Tilia* plants, particularly in the context of cancer treatment. Continued

investigation into the isolation, characterization, and mechanistic understanding of these compounds could pave the way for the development of new and effective anticancer therapies. The promising results from these initial studies underscore the need for more comprehensive research to fully realize the therapeutic potential of *Tilia* species.

7.4 Antitumor and antiproliferative activity

Davicino *et al.*^[48] conducted a study on the immunomodulatory effects of AE and dichloromethane extract (DM) from *Tilia × viridis*, a species commonly used in Argentina, on murine lymphocyte proliferation. Their findings indicated that both extracts stimulated lymphocyte proliferation. Specifically, the DM extract primarily activated macrophages, while the AE extract directly influenced lymphocytes, a result attributed to the presence of rutin. Additionally, the DM extract showed potential in modulating immune cells, suggesting a viable strategy for enhancing resistance against malignancies and infectious diseases. This study builds on previous research by Davicino *et al.*^[49], which identified *Tilia × viridis* as a source of antioxidants capable of inhibiting tumor cell proliferation. Further research by Kim *et al.*^[50] explored the anticancer properties of methanol extract from the trunks of *T. amurensis* Rupr. This extract inhibited nitric oxide formation in murine microglial cells and led to the discovery of a new isoflavonoid glycoside, alongside 16 known compounds, which exhibited modest anticancer activity. Hassanien *et al.*^[51] advanced this field by developing a cost-effective method for synthesizing copper nanoparticles (Cu-NPLs) using *Tilia* extract. These nanoparticles proved effective against several pathogens and displayed cytotoxicity against various human cancer cells, highlighting their significant potential in cancer therapy. In another study, Jabeur *et al.*^[52] investigated the antioxidant, anti-inflammatory, and anticancer properties of hydroethanolic extracts from *T. platyphyllos* Scop., known for their rich phenolic compound content. The extracts showed a high ratio of flavonoids to phenolic acids, with protocatechuic acid and epicatechin being the most abundant. These compounds demonstrated significant inhibition of lipid peroxidation and exhibited noteworthy antitumor activity. Collectively, these studies underscore the significant antitumor and antiproliferative potential of various *Tilia* L. extracts. The research demonstrates that *Tilia* extracts can stimulate immune responses, inhibit tumor cell proliferation, and possess antioxidant and anti-inflammatory properties. The identification of bioactive compounds, such as rutin, isoflavonoid glycosides, and phenolic acids, further highlights the therapeutic promise of *Tilia* L. in cancer treatment. These findings suggest that *Tilia* L. holds considerable potential for the development of novel anticancer therapies, warranting further investigation to fully elucidate its mechanisms and optimize its applications in clinical settings.

7.5 Antioxidant activity

Charpentier *et al.*^[53] investigated the antioxidant and phytochemical properties of *T. tomentosa* concentrated bud macerates using radical scavenging assays. They successfully isolated glycosylated flavonoids, nucleosides, and phenolic acids, reinforcing the phytochemical relevance of *T. tomentosa* in gemmotherapy. Mainente *et al.*^[54] examined the stability of total phenols, flavonols, and antioxidant potential in *T. tomentosa* Moench flower extracts, also evaluating their contractile effects on intestines in a mouse model. Their findings confirmed the

biological activity and bioavailability of these flavonols. Rodriguez-Magana *et al.*^[55] focused on the hypoglycemic and antioxidant activities of *T. americana* methanolic extracts in diabetic rats. This study highlighted the potential therapeutic benefits of these extracts in managing diabetes through their antioxidant properties. Sharma *et al.*^[56] explored the antioxidant properties, phenolic, and flavonoid contents of methanol extracts from the stems and bark of *Tilia europaea* L. Notably, the stem bark of *T. europaea*, indigenous to the northwestern Indian Himalayas, exhibited significant ABTS radical scavenging activity, attributed to its rich natural component composition. Alasalvar and Cam^[57] utilized pressurized hot water extraction to extract phenolics from linden for iced tea production, finding that the phenolic content and antioxidant activity were comparable to those of microencapsulated linden powders. The anti-wrinkle properties and chemical constituents of ethanol extracts from *T. taquetii* Schneider leaves, discovering a high concentration of triterpenes that show promise as effective ingredients in anti-wrinkle cosmetic products. Furthermore, Lianza *et al.*^[58] noted that *T. platyphyllos* extract, rich in flavonoids and phenolic compounds, exhibits significant antioxidant properties and tyrosinase inhibition, making it a valuable target for cosmetic and dermatological applications. Overall, the various studies underscore the robust antioxidant activity of different *Tilia* species, highlighting their potential applications in gemmotherapy, diabetes management, and cosmetic industries. The high levels of phenolic and flavonoid compounds in *Tilia* extracts contribute to their efficacy as natural antioxidants, providing therapeutic benefits across multiple domains.

7.6 Antinociceptive and antispasmodic efficiency

The pharmacological properties of *Tilia* species have been extensively studied for their potential therapeutic applications, particularly focusing on their antinociceptive and antispasmodic effects. Martinez *et al.*^[59] conducted a comprehensive assessment of the antinociceptive effects of hexane, methanol, and AE from the inflorescences of *T. americana* var. *mexicana* using a rat model with induced functional impairment. The study demonstrated that all three extracts effectively suppressed pain responses. The underlying mechanism was linked to the interaction with serotonin receptors, and the presence of quercetin was identified as a significant contributor to this pharmacological activity. Expanding on the antispasmodic properties of *Tilia*, Cerantola *et al.*^[60] investigated the effects of *T. tomentosa* Moench flower extract on the contractility of the small intestine. Using a mouse model, the study measured the tension in intestinal muscles to evaluate the extract's efficacy in treating intestinal disorders. The findings confirmed that the flower extract exhibited notable antispasmodic activity, supporting its traditional use in alleviating intestinal discomfort. Additionally, Cardenas-Rodriguez *et al.*^[61] explored the anticonvulsant activity of *T. americana* var. *mexicana* extracts, with a particular focus on the methanol extract from the inflorescences and leaves. Using spectrophotometric analysis, they identified key flavonoids such as isoquercitrin, quercetin, and rutin, which exhibited strong antioxidant properties. These flavonoids were highlighted for their potential in treating central nervous system disorders due to their ability to mitigate oxidative stress. In summary, the extracts of *Tilia* species, demonstrate significant antinociceptive and antispasmodic properties. The effectiveness of these extracts is attributed to their interaction with serotonin receptors and the presence of bioactive flavonoids like quercetin, isoquercitrin, and

rutin. These findings underscore the therapeutic potential of *Tilia* extracts in managing pain, intestinal disorders, and central nervous system conditions.

7.7 Anxiolytic, antidepressant, and sedative activity

Martinez-Hernandez *et al.*^[62] conducted a detailed investigation into the pharmacological effects of metabolites derived from the aglycone quercetin, particularly those from the metabolism of *T. americana* var. *mexicana*. Their research demonstrated that flavonoid-rich fractions exhibited significant behavioral activity in mice. This study builds on earlier work by Aguirre-Hernandez *et al.*^[63], who analyzed inflorescences from Mexican native *Tilia* species, focusing on *T. americana* var. *mexicana*. Samples from three different regions in Mexico were assessed for flavonoid content and anxiolytic-like reactions using HPLC-MS. The results showed anxiolytic-like responses to aglycons of quercetin and kaempferol, reinforcing the traditional use of *Tilia* inflorescences in Mexican folk medicine for their anxiolytic properties. Bianco *et al.*^[64] highlighted the widespread use of linden flower tea as a sedative across various countries, indicating its long-standing traditional use. In line with this, Allio *et al.*^[65] explored the sedative and anxiolytic effects of *T. tomentosa* Moench bud extracts on hippocampal neurons, finding significant sedative effects. Further, Nogueron-Merino *et al.*^[66] examined the anxiolytic properties of the bracts and flowers of *T. americana* var. *mexicana*, discovering dose-dependent anxiolytic effects linked to flavonoids such as tilirosid, quercetin glucoside, quercitrin, rutin, and kaempferol. These effects were attributed to their interaction with the serotonergic system. Turrini *et al.*^[67] confirmed the efficacy of *T. tomentosa* Moench bud extracts as dietary supplements with anxiolytic properties, noting that the responses varied with age and gender. Juarez Ramirez *et al.*^[68] provided additional support by evaluating the anxiolytic fraction of *T. americana*, standardized for various flavonoids. Chavez-Morales *et al.*^[69] extended this research to assess the antidepressant effects of *T. americana* fractions and tilirosid in rats. They found that all tested fractions exhibited antidepressant activity, with organic fractions also demonstrating sedative effects. These findings confirm the traditional medicinal use of *Tilia* species and indicate potential for developing standardized *Tilia* extracts as therapeutic agents. The evidence demonstrates the efficacy of *Tilia* extracts in modulating behavioral responses, with specific effects linked to the serotonergic system.

7.8 Neuroactive and hepatoprotective properties

The neuroactive and hepatoprotective properties of *Tilia* L. have garnered significant attention due to their potential therapeutic applications. Several studies have focused on isolating and analyzing bioactive compounds from various *Tilia* species, elucidating their effects on the central nervous system and liver protection. Loscalzo *et al.*^[70] conducted a comprehensive analysis of the neuroactive constituents in the ethanol extract of *T. petiolaris* DC's inflorescence. They successfully identified three glycosides: kaempferol 3-*O*-glucoside-7-*O*-rhamnoside, quercetin 3-*O*-glucoside-7-*O*-rhamnoside, and isoquercitrin. Among these, quercetin 3-*O*-glucoside-7-*O*-rhamnoside demonstrated significant depressant action, indicating its potential as a neuroactive flavonoid glycoside. In another study, Lee *et al.*^[39] explored the neuroprotective properties of *T. amurensis*. Through bioactivity-guided fractionation, they isolated compounds including β -D-fructofuranosyl, α -D-glucopyranoside, epicatechin,

nudiposide, lyoniside, and scopoletin. Notably, epicatechin, nudiposide, lyoniside, and scopoletin exhibited protective effects against glutamate-induced neurotoxicity, highlighting their potential in neuroprotection. *T. americana*, widely used in Mexico for its central nervous system benefits, was studied by Angeles-Lopez *et al.*^[71,72] for its neuroprotective effects against brain ischemia in mice. Their results showed that both nonpolar and polar extracts of *T. americana* increased survival rates, improved neurological functions, and reduced infarct areas compared to the ischemic group, thus showcasing its neuroprotective capabilities. In Mexican traditional medicine, *T. americana* var. *Mexicana* is used to treat mild mental tension and promote relaxation, as noted by Martinez-Hernandez *et al.*^[62]. It is also utilized for inducing sleep, alleviating anxiety, headaches, mood disorders, and discomfort. The hepatoprotective properties of *Tilia* L. were highlighted in a study by Yayalaci *et al.*^[73], which examined the effects of linden flower infusion against ethanol-induced oxidative stress in rats. They assessed various liver damage biomarkers and antioxidant defense systems, demonstrating the infusion's protective and antioxidant effects on the liver. Additionally, Coballase-Urrutia *et al.*^[74] evaluated the antioxidant, neuroprotective, and hepatoprotective activities of organic and AE from *T. americana* var. *Mexicana* foliage. Their findings suggest potential pharmaceutical and local health benefits, proposing these extracts as candidates for further development in therapeutic applications. Ferreira *et al.*^[75] investigated *T. platyphyllos* Scop. extract for its antioxidant, anti-inflammatory, and anticancer activities. While their findings suggested a degree of safety, they also emphasized the importance of considering the extract's toxicity levels. *Tilia* L. exhibits promising neuroactive and hepatoprotective properties across various species. The neuroprotective effects are largely attributed to specific flavonoid glycosides and other compounds that mitigate neurotoxicity and support neurological health. The hepatoprotective benefits, demonstrated through studies on oxidative stress and liver damage biomarkers, highlight the potential of *Tilia* L. in liver protection. However, further research is essential to fully understand the safety, efficacy, and therapeutic potential of *Tilia* extracts. The comprehensive investigation into these properties holds significant promise for developing novel treatments for neurological and hepatic conditions, leveraging the natural bioactive compounds found in *Tilia* L.

7.9 Anti-inflammatory activity

Czerwinska *et al.*^[76] conducted an extensive investigation into the composition and biological effects of flavan-3-ol derivatives found in infusions made from *T. cordata* flowers. Their research focused on isolating and identifying the principal procyanidins present in the flowers and evaluating their impact on the inflammatory response of human neutrophils in an *ex vivo* setting. Through meticulous phytochemical analysis, 10 compounds were identified and isolated. The study further examined the anti-inflammatory potential of these substances, revealing that infusions from lime flowers have traditionally been effective in mitigating inflammation and mucosal irritation, particularly in cases of the common cold, pharyngitis, and tonsillitis. In parallel, Georgiev *et al.*^[77] explored the flowers of silver linden, emphasizing the presence of various immunomodulatory pectins. Their findings indicated that these pectins could induce the production of reactive oxygen species (ROS) and nitric oxide (NO), which are indicative of the anti-inflammatory properties associated with silver linden extracts. The combined research from both studies

underscores the significant anti-inflammatory activity of *Tilia* species. These compounds contribute to the modulation of the inflammatory response, supporting the traditional use of linden flower infusions in treating respiratory and mucosal inflammations. The potential of these natural extracts in developing therapeutic agents aimed at controlling inflammation and enhancing immune response.

8 Ecological functions and conservation

The genus *Tilia*, commonly known as linden, is extensively used in landscaping due to its aesthetic attributes. These trees are widely planted as hedges, street trees, and landscape trees in Europe and North America, praised for their elegant form, significant height, broad leaves that provide substantial shade, longevity, fragrant flowers, and resilience to pests, diseases, pollution, and harmful gases. Their versatility makes them ideal for various environments, including parks, gardens, streets, and industrial or mining areas.

In Central and Northwestern European countries, *Tilia* L. are particularly prominent in urban landscapes. They exhibit notable resistance to heavy metals and salinity, facilitated by their symbiotic relationship with ectomycorrhizal fungi, which protect them from these environmental stressors^[78]. Urban soil contamination with heavy metals poses significant risks to public health and reduces the survival rate of urban trees. For instance, the quality and chlorophyll levels of *T. tomentosa* leaves have been used to assess cadmium and lead pollution in soils^[79]. Several studies have further examined the interaction between *Tilia* L. and environmental pollutants. Markovic *et al.*^[80] analyzed the annual rings and bark of *T. platyphyllos* from four Serbian sites, finding that Mn and Pb concentrations in the tree rings closely correlated with the bioavailable element ratios in the soil. Erofeeva^[81] investigated the impact of vehicular pollution on guaiacol peroxidase activity and lipid peroxidation in *Tilia* × *europaea* leaves. Similarly, Mantovani *et al.*^[82] collected PM10 filters and *T. cordata* leaves over five months and used scanning electron microscopy and energy dispersive spectrometer (SEM-EDS) to analyze their surface and internal composition. They discovered that magnetite particles, primarily from traffic pollution, accumulated on the leaf surface, indicating their potential as environmental indicators. Additionally, Kowalski and Frankowski^[83] studied mercury concentrations in soil, buds, and leaves of *T. platyphyllos* over four growing seasons, identifying atmospheric deposition as the primary source of mercury in the leaves. Popek *et al.*^[84] explored the deposition of particulate matter, including heavy metals and polycyclic aromatic hydrocarbons, on *T. cordata* leaves, highlighting the species' capacity to improve urban air quality. Furthermore, Van Geel *et al.*^[85] found that soil pH, organic matter, and moisture significantly influenced the ectomycorrhizal fungal populations associated with *T. tomentosa*, which in turn enhanced urban tree health. The diversity of ectomycorrhizal fungi in *Tilia* species was shown to improve species richness and resilience^[86,87]. Collectively, these studies demonstrate that *Tilia* L. possess substantial resistance to air and soil pollution, making them valuable indicators for assessing urban environmental quality. Their presence contributes significantly to improving urban living conditions and mitigating adverse effects on human health.

Natural ecosystems offer a conducive habitat for various *Tilia* L. species, including those that are endemic, endangered, and threatened, underscoring their considerable conservation

importance. Canturk and Kulac^[88] predicted future distribution changes for three economically, ecologically, and socially valuable linden species in Turkey—*T. tomentosa*, *T. cordata*, and *T. platyphyllos*—using models, and found that their distribution areas will significantly shrink. Additionally, selective logging is accelerating the succession of *T. amurensis* secondary forests^[89]. Given that some endemic linden species are currently endangered or threatened, their conservation is of paramount importance. *T. miqueliana* Maxim., endemic to eastern China and first identified in Nanjing, typically grows on mountain slopes, in ravines, or open forests. Its presence is primarily noted in the Chinese provinces of Zhejiang, Anhui, Jiangxi, and Guangdong, as well as in Japan. This species is rare and endangered, with few locations in East China hosting wild colonies exceeding 30 plants. The largest known natural colony, consisting of hundreds of *T. miqueliana* Maxim. specimens, is located on Niushou Mountain in Nanjing^[90]. Wu and Shen^[91] demonstrated that the H₂SO₄-GA₃ cold stratification treatment significantly enhances dormancy release and germination rates in *T. miqueliana* Maxim. seeds. Germination is typically slow, often requiring up to 2 years post-sowing due to the seeds' hard shell, which poses a challenge for degradation. Consequently, hulling and swelling are necessary for successful germination. This difficulty in seed germination has been linked to the decline of wild *T. miqueliana* Maxim. populations^[92].

Table 2 lists the endangered status of some *Tilia* L. species. The threat categories are used by the International Union for Conservation of Nature (IUCN) to classify species based on their risk of extinction. Species classified as Least Concern (LC) are those that have been evaluated and found to be at low risk of extinction. Vulnerable (VU) species are those considered to be facing a high risk of extinction in the wild. Data deficient (DD) is a category used when there is inadequate information to make a direct, or indirect, assessment of a species' risk of extinction. The information comes from International Union for Conservation of Nature (IUCN) Red List Categories and Criteria^[93].

9 Conclusion

The genus *Tilia* L., a member of the Malvaceae family, possesses significant edible, medicinal, economic, and ecological value. This review synthesizes the research progress on *Tilia* in genetic and phylogenetic analysis, phytochemistry, edible value, pharmacology, and ecological conservation. *Tilia* species have large and complex genomes, but whole-genome sequencing has yet to be completed. Current research primarily focuses on chloroplast and plastid genomes. Various parts of *Tilia*, including leaves, flowers, and seeds, are edible and contain numerous bioactive compounds such as flavonoids, terpenoids, phenolic acids, and lignan glycosides. These compounds exhibit a wide range of biological activities, including anti-inflammatory, antioxidant, anticancer, and neuroprotective effects. *Tilia* species are also valued for their aesthetic appeal and pollution resistance, making them widely used in urban landscapes. They play a crucial role in improving urban air quality by absorbing heavy metals and other pollutants. However, some *Tilia* species face threats of extinction or population decline due to habitat loss and challenges in seed germination, making conservation efforts essential, especially for endemic and threatened species. Comprehensive research on the phytochemistry and pharmacology of *Tilia* reveals its immense potential in the development of new drugs and functional foods. Bioactive compounds from *Tilia* have shown

Table 2 Threatened species of *Tilia* listed in International Union for Conservation of Nature (IUCN) (2022–2)

Serial No.	Name of the taxa	Threat category	Population status	Scope of assessment
1	<i>T. platyphyllos</i>	LC	Decreasing	Global & Europe
2	<i>T. cordata</i>	LC	Decreasing	Global
3	<i>T. tomentosa</i>	LC	Unknown	Global
4	<i>Tilia callidonta</i>	VU	Unknown	Global
5	<i>T. japonica</i>	LC	Unknown	Global
6	<i>T. chingiana</i>	LC	Unknown	Global
7	<i>T. maximowicziana</i>	LC	Unknown	Global
8	<i>T. oliveri</i>	LC	Unknown	Global
9	<i>T. kiusiana</i>	LC	Unknown	Global
10	<i>T. dasystyla</i>	LC	Unknown	Global
11	<i>T. amurensis</i>	LC	Decreasing	Global
12	<i>T. nobilis</i>	LC	Unknown	Global
13	<i>T. americana</i>	LC	Stable	Global
14	<i>T. endochrysea</i>	LC	Unknown	Global
15	<i>T. mandshurica</i>	LC	Decreasing	Global
16	<i>T. miqueliana</i>	DD	Unknown	Global
17	<i>T. paucicostata</i>	LC	Unknown	Global
18	<i>T. caroliniana</i>	LC	Stable	Global
19	<i>T. chinensis</i>	LC	Unknown	Global
20	<i>T. tuan</i>	LC	Stable	Global
21	<i>T. henryana</i>	LC	Decreasing	Global
22	<i>T. mongolica</i>	LC	Unknown	Global
23	<i>Tilia concinna</i>	DD	Unknown	Global
24	<i>Tilia breviradiata</i>	LC	Unknown	Asia
25	<i>Tilia chenmoui</i>	VU	Decreasing	Asia
26	<i>T. hupehensis</i>	DD	Unknown	Asia
27	<i>Tilia integerrima</i>	DD	Unknown	Asia
28	<i>Tilia intonsa</i>	LC	Unknown	Asia
29	<i>Tilia kueichouensis</i>	LC	Unknown	Asia
30	<i>Tilia laetevirens</i>	DD	Unknown	Asia
31	<i>Tilia lepidota</i>	LC	Unknown	Asia
32	<i>Tilia likiangensis</i>	LC	Unknown	Asia
33	<i>Tilia membranacea</i>	LC	Unknown	Asia
34	<i>Tilia mesembrinos</i>	DD	Unknown	Asia
35	<i>Tilia mofungensis</i>	DD	Unknown	Asia
36	<i>Tilia nanchuanensis</i>	DD	Unknown	Asia
37	<i>Tilia oblongifolia</i>	DD	Unknown	Asia
38	<i>Tilia obscura</i>	DD	Unknown	Asia
39	<i>Tilia omeiensis</i>	DD	Unknown	Asia
40	<i>Tilia populifolia</i>	LC	Stable	Asia
41	<i>Tilia tristis</i>	LC	Stable	Asia
42	<i>Tilia yunnanensis</i>	LC	Stable	Asia

promising results in various therapeutic applications. For example, flavonoids and phenolic acids from *Tilia* have demonstrated significant antioxidant and anti-inflammatory properties, which could be harnessed for developing treatments for cardiovascular diseases and neurodegenerative disorders. Furthermore, the neuroprotective effects of compounds such as terpenoids and lignan glycosides suggest potential applications in preventing and treating conditions like Alzheimer's disease and other cognitive disorders. These compounds can modulate inflammatory pathways and protect neuronal cells from oxidative stress. In the

realm of functional food development, *Tilia* extracts can be incorporated into various food products to enhance their health benefits. For instance, the inclusion of *Tilia* bioactive compounds in functional foods could help in managing chronic diseases such as diabetes, hypertension, and obesity by leveraging their bioactive properties to modulate metabolic pathways and improve overall health. Future research directions include whole-genome sequencing to identify key genes regulating the synthesis of bioactive compounds and enhance the understanding of their therapeutic mechanisms. Continuous isolation and identification

of bioactive compounds from *Tilia* are crucial for developing targeted therapies and validating traditional uses. Clinical trials and safety assessments of *Tilia* extracts are vital to evaluate their efficacy and safety in human populations, which is essential for their potential medicinal applications. Finally, conservation and sustainable utilization of *Tilia* are necessary to ensure the protection of endangered species and promote sustainable harvesting practices. This will support the long-term availability of these valuable plant resources. By focusing on these areas, future research can fully exploit the medicinal and edible potential of *Tilia*.

Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

Acknowledgements

This work was funded by the Jiangsu graduate research innovation program (No. KYCX23_1253).

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