A Minireview on Chemical Constituents and Bioactivities of *Lindera glauca*

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Abstract *Lindera glauca* (Sieb. et Zucc.) Bl is Chinese herbal medicine known as Niu-jin tree or Leigongzi. Alkaloids, flavonoids, terpenes, volatile oils, etc., are found in *L. glauca*, exhibiting some pharmacological activities such as anti-bacterial, anti-influenza virus, anti-fungal, antioxidant activities, an effect on bronchial and intestinal smooth muscle, and so on. Herein, we summarized chemical compositions and physiological activities of *L. glauca* for future research.

Keywords *Lindera glauca*, chemical constituents, bioactivities

Introduction

*Lindera glauca* (Sieb. et Zucc.) Bl, belonging to the genus *Lindera* (Lauraceae), is a deciduous shrub or small tree. It grows in roadsides, forest margins, hills below 900 meters altitude, distributed in China, Indochina, Korea, Japan and other places.[5] Modern pharmacological research shows that its roots, branchlets, leaves and fruits can be used medicinally.[5] Based on the above effects, most research on its chemical constituents and bioactivities have been increasingly comprehensive. In this paper, we reviewed chemical composition and structures of *L. glauca*.

Chemical constituents of *L. glauca*

The chemical compositions of the roots, leaves and fruits of *L. glauca* mainly include alkaloids, flavonoids, terpenes, volatile oils, and other compounds. Essentially, it is consistent with the components of *Lindera*.[3]

Alkaloid constituents

The alkaloids are the primary compositions in *L. glauca*, in particular isoquinoline alkaloids and aporphine alkaloids (Figure 1).

In 1984, Kozuka et al. isolated two aporphine alkaloids and two tetrahydroisoquinoline alkaloids from *L. glauca*, named laurotetanine (1), N-methyllaurotetanine (2), (+)-retriculine (3), and (+)-norcinnamolaurine (4).[4] In 2001, Chang et al. first isolated 28 compounds from *L. glauca*, including seven alkaloids, (+)-3-chloro-N-formylnornantenine (5), (+)-N-formyl-nornantenine (6), (+)-baldine (7), (+)-norbaldine (8), (+)-nor-4-baldine (9), lycicamine (10), tetrahydroberberine (11), in which (+)-3-chloro-N-formylnornantenine (5) is a new compound.[5] Then, six amides, named *N*-cis-sinapoyltyramine (12), *N*-trans-sinapoyltyramine (13), *N*-cis-feruloyltyramine (14), *N*-trans-feruloyltyramine (15) and *N*-p-coumaroyltyramine (16), squamolone (17), two morphinandienones, (+)-*N*-methyl-flavimantian (18) and pallidine (19), three aporphines, (+)-isobaldine (20), (+)-norisocorydine (21) and (+)-laetanine (22), were isolated and identified, in which compound 12 is a new compound.[6] In 2016, Ting et al. isolated magnocurarine (23) from *L. glauca* root for the first time.[7] Liang et al.
separated laurolitsine (24), (+)-flavinantine (25) and norpredicentrine (26) from *L. glauca*.[8]

**Flavonoids**

Flavonoids are also one of the main components of *L. glauca* (Figure 2).

![Figure 2](image-url) The structures of flavonoid compounds isolated from *L. glauca*.

Four flavonoids, kaempferol (27), kaempferol-3-O-arabinoside (28), quercetin (29) and quercetin-3-O-rhamnoside (30), were obtained from the methanol extract of *L. glauca* by Chang *et al.*[9] Eight flavonoids were isolated by Huha *et al.* from *L. glauca* and identified as lindeglaucone (31), lindeglaucol (32), cinnamtannin B1 (35), cinnamtannin D1 (37), and procyanidin A1 (38); their antioxidant activities were analyzed.[9] Park has reported several catechinic acids, such as (+)-catechin (39), (-)-epicatechin (40), epigallocatechin (41), 5,3'-di-O-methyl-(-)-epicatechin (42) and 2R,3R,5,6,7,4'-pentahydroxylavanonol (43). These isolated compounds were tested against HRV1B, CVB3, and PR8-infected Vero cells for their antiviral activities.[10] Liang *et al.* isolated procyanidin B2 (44) and epicatechin-(2β-O-7,4β-8)-entcatechin-(4β-8)-epicatechin (45) from *L. glauca*.[8]

**Terpenoids and volatile oil**

The terpenoid components of *L. glauca* contain monoterpenes, sesquiterpenes, triterpenes, *etc.* A significant component of *L. glauca* is essential oil, which has a large array of physiological functions (Figure 3). Pseudoguaianelactones A—C (46—48) were separated from the root of *L. glauca*, which have significant anti-inflammatory activity.[11] In 1972, Komaea *et al.* separated three essential oil named 1,8-cineole (49), caryophyllene (50), bornyl acetate (51), respectively.[12] In 1982, Liu *et al.* isolated and identified 13 components from the fruits[13] and 34 components from the leaves of *L. glauca*, revealing that ocimene was the main component of the essential oil in the fruits of *L. glauca*.[14]

![Figure 3](image-url) The structures of terpenoid and volatile oil compounds isolated from *L. glauca*. 
In 2012, Wan et al. extracted 36 volatile oil from L. glauca by steam distillation and identified by GC-MS. Among the 36 components identified, the main components are ocimene (52), β-caryophyllene (53), citral (54) and linalool (55).

In 2013, You et al. extracted 60 volatile oil from the fruit of L. glauca and identified the chemical components by GC-MS, including β-myrcene (56), D-limonene (57), eucalyptol, linalool, citronellal (58), citral (59), and β-caryophyllene. Among them, citral had the highest content with antibacterial and anti-inflammatory effects; limonene showed antibacterial, expectorant, antilusive and antiasthmatic effects; β-caryophyllene exhibited a strong antibacterial effect. These components are the main active components of the volatile oil of L. glauca fruit. The volatiles of L. glauca fruits with different maturities were isolated by hydro-distillation method and analyzed by GC-MS, comprising β-ocimene, α-pinene (60) and β-caryophyllene.

Other compounds

In addition to the above compounds, butanolides, lignans, diarylpropanoic and phenylpropionic acids have been reported in L. glauca (Figure 4).

Seki and his team identified two new methoxybutanolides compounds from the roots and stems of L. glauca, named (3S,2E)-2-(11-dodecenyldiene)-3-methoxy-4-methyl-enebutanolid (61) and (3S,2E)-2-(11-dodecenyldiene)-3-methoxy-4-methylenebutanolide (62). Then, they isolated ten new butanolides compounds, linderanolid A—E (63—67) and isolinderanolid A—E (68—72).

Chang and his team identified a butanolide (akolactone A, 73), a p-quione (2,6-dimethoxy-p-quione, 74), with six benzenoids, methylparaben (75), p-hydroxybenzoic acid (76), vanillic acid (77), syringic acid (78), 3,4,5-trimethoxybenzoic acid (79), and 3-(3,4-dihydroxyphenyl) propionic acid (80), and six steroid compounds, β-sitosterol (81), β-sitostenone (82), stigmasta-4,22-dien-3-one (83), 6β-hydroxy-β-sitostenone (84), 6β-hydroxystigmastane (85), and β-sitosteryl-D-glucoside (86), from L. glauca.

Suha et al. isolated three new lignans derivatives, named linderanoides A—C (87—89), and five known lignans from the solvent site of Ethyl acetate, in which 87 was selectively toxic to A498 cells. Parka et al. isolated and identified a new lignan, (−)-9-O-E-feruloyl-lyoniresinol (90). A new cerebroside, glaucerubeside (91), was isolated and identified from the branches of L. glauca by Jae-Yu et al. Park et al. found two new diarylpropanoic (2S)-3′,4′,4′-dihydroxy-2′,3′,6′-trimethoxy-1,3-diarylpropan-2-ol (92) and 4′,4′-dihydroxy-3′,6′-dimethoxy-2′-O-β-D-glucopyranosyl-1,3-diarylpropan-2-one (93). Huh extracted three new diarylpropanoids from the L. glauca, named Lindeglaucol (94), Lindeglaucone (95), and Lindeglaucoside (96).

Bioactivities

L. glauca is a traditional Chinese medicinal plant with a variety of pharmacological activities such as anti-bacterial, anti-inflammatory, antioxidative effect, and so on.

Anti-bacterial, anti-influenza virus and anti-fungal activities

Liu et al. examined the bioactivity of the essential oil extracted from the leaves of L. glauca. It has anti-influenza virus activity in chicken embryos and titer of 1 : 80, antibacterial activity against Pneumococcus/Staphylococcus albicans, Neisseria cattarrhalis/Bacillus anthracis/Pseudomonas aeruginosa/Bowie Freund/Dysentery sonnei, and antifungal properties against Cryptococcus neoforms and Candida albicans. Yu et al. reported that the extracts of L. glauca had...
antibacterial activity, and they were more selective on Gram-positive bacteria and mold than on Gram-negative bacteria and yeast.[22]

**Antioxidation**

Zhang et al. found that the leaves of *L. glauca* could effectively clean free radicals and have certain antioxidant activity *in vitro*. The free radical scavenging rate is equal to 67.92% of vitamin C when the concentration is 30 times. When the concentration is 40 times that of butyl hydroxyanisole, the free radical scavenging rate is 58.60%.[21]

**Improvement of the inflammatory response in spinal cord injury area**

Cheng disclosed that the transplantation of bone marrow combined with *L. glauca* leaf extract could successfully heal damaged areas of spinal cord, which was attributed to the decrease in inflammatory reaction induced by the necrosis factor of the tumor.[23]

**Anti-tumor cell proliferation activity**

Liu et al. found that the alkaloids in *L. glauca*, N-methylaurtetanine, laur odorantiane, and (+)-boldine, had a significant effect on the proliferation of four human tumor cells: HT-29, SGC-7901, SMMC-7721 and A549. Among them, N-methylaurtetanine had strong inhibitory activity on the proliferation of HT-29 and SGC-7901 cells, with IC50 values of 8.68 ± 0.38 μg/mL, 18.32 ± 2.64 μg/mL, respectively.[22]

**Inhibitory activities *in vitro* and *in vivo* on glucosidase**

Cao et al. observed that the fractions of *L. glauca* could inhibit the activity of glucosidase *in vitro* and *in vivo*. The IC50 values of petroleum ether, ethyl acetate and n-butanol for inhibiting yeast α-glucosidase are 229.70, 259.10, 165.80 μg/mL, respectively; only the ethyl acetate part can inhibit the α-glucosidase activity of rat small intestine with IC50 = 418.17 μg/mL.[24]

**Relaxation of bronchial and intestinal smooth muscle activity**

Liu et al. found that the essential oil of *L. glauca* leaves had sedative and hypnotic effects, relaxation of bronchial and intestinal smooth muscle, etc.[14]

**Conclusion and Perspective**

As traditional Chinese medicine, *L. glauca* is distributed widely with long medicinal history. The chemical constituents of *L. glauca* include alkaloids, flavonoids, terpenes volatile oils, and other compounds. The studies on *L. glauca* demonstrated that it has a spectrum of pharmacological effects. At present, the research on *L. glauca* is mostly focused on the components and functions of alkaloids, and its other components and bioactivities need to be further studied.

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**Conflict of Interest**

The authors declare no conflict of interest.

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