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## 2 ***Liquidambar formosana* Hance: a mini-review 3 of Chemical Constituents and Pharmacology**

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**ABSTRACT**

Aims: *Liquidambar formosana* Hance is of great an arbor with ornamental, medicinal and economic values. Its' various organs, such as the fruit, leaf, resin, have high medicinal and economic values and commonly used in the pharmaceutical, food and cosmetic industries. Currently, several studies aimed at isolation and identification of active constituents of *L. formosana* and its pharmacological actions of different plant parts based on the treatment of several diseases. The main objective of this paper is to review recent advances of *Liquidambar formosana* Hance in chemical constituents and pharmacology during the last two decades, in an attempt to provide useful references for plant drug studies.

Methodology: Information on *L. formosana* from journals and books published during the last two decades was collected based on worldwide accepted scientific databases via an electronic search (PubMed, Elsevier, Google Scholar, Springer, Web of Science and CNKI).

Results: The detailed phytochemical composition with respect to the pharmacological properties of different parts of this multipurpose tree. Trace elements, volatile oils, terpenoids, phenylpropanoids, and flavonoids and tannins constituents are the natural plant secondary metabolites known from the different organs of *L. formosana*. The main pharmacological actions of *L. formosana* and compounds isolated therefrom include antitumor, antithrombotic, antimicrobial, antiviral, antiinflammatory antidepressant, and antioxidant actions. *L. formosana* leaves are a strong anti-oxidant substance and may either mitigate or prevent generation of free radicals.

Conclusion: Many pharmacological activities appear to be attributable to terpenoid and to the flavonoid constituents; terpenoids are also reported to be responsible for the antitumor antimicrobial, and antiviral activities that had been documented for *L. formosana*. Based on the foundation of chemical constituents, their possible contribution to the demonstrated efficacy of extracts obtained from *L. formosana* are suggested, as well as new directions on quality control and application of this plant are suggested. These biologically active compounds are also be determined quantitatively by HPLC analysis, which can be used to control the quantity of this plant. *L. formosana* will be further developed as medicinal and economic values, and thereby promote its cultivation. Further research is required to isolate and identify more new compounds contribute to the pharmacological effects.

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18      *Keywords: Liquidambar formosana* Hance, *Chemical constituents, Pharmacological*  
19      *properties, Research progress*

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23      **1. INTRODUCTION**

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25      Plants of the genus *Liquidambar* as traditional Chinese and Ayurvedic medicines are  
26      distributed mainly in Southeast Asia and America, but they have been cultivated in many  
27      countries around the world as ornamental plants. The genera contains four species, that is, *L.*  
28      *styaciflora* (known as American sweet gum), *L. orientalis* Mill. (Oriental sweet gum), *L.*  
29      *formosana* Hance (Chinese sweet gum) and *L. acalycina* H.T. Chang (Chang's sweet gum)  
30      [1]. *L. formosana* Hence (also known as maple), one of the genus *Liquidambar*, is a tall  
31      deciduous tree widely distributed in various regions of the south of the Qinling Mountains  
32      and Huaihe River in China, and also found in northern Vietnam, Laos and South Korea. *L.*  
33      *formosana* is a famous ornamental plant for leaves are green in spring and summer, and red  
34      in autumn. Different plant parts of *L. formosana*, such as the leaf, fruit, bark, and resin, are  
35      proved to be the treasures as natural medicinal plant resources (Figure 1). Its leaves have  
36      the effects of relieving pain, detoxification, and hemostasis. It can be used for the treatment  
37      of acute gastroenteritis, dysentery, postpartum wind, infantile tetanus, carbuncles hair back,  
38      and so on. Its fruits (also known as Lulutong, Jiukongzi, *Fructus liquidambaris*), have been  
39      used as a traditional Chinese medicine in China (TCM) for thousands of years. It can treat  
40      joint arthralgia, numbness cramps, edema, puffiness, and so on. Aromatic essential oils from  
41      *L. formosana* resin (known as balsam) have been widely used for both medicinal and  
42      cosmetic purposes. This resin as an expensive TCM has been used traditionally for the  
43      treatment of flutter injury, ulcer throat, vomiting, epistaxis, and trauma bleeding in China [2].

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45

46      **Fig. 1 *L. formosana* and its' various organs**

47 As a kind of natural pigment resources, *L. formosana* has great potential in foods and  
48 cosmetics industry. Leaves of *L. formosana* have been taken as a rice dye for festival food  
49 by a small group of people in Guangxi province, a southern province of China. Moreover, *L.*  
50 *formosana* can be taken advantage of landscaping and xerogardening as an ornamental  
51 plant, and improve the soil structure in ecology [3]. Therefore, *L. formosana* has a good  
52 potential prospect for development because of its' medicinal, economic, ecological and  
53 ornamental values.

54 However, shape of *L. formosana* resin is similar to that of pine rosin, which is often given the  
55 opportunity for unscrupulous traders to misdescribe two resins. In addition, as the big culture  
56 country of *L. formosana*, there are a lot of leaves, fruits, and barks as the offal abandon in  
57 the field but not to fully utilized every year in rural area. So far no comprehensive review has  
58 been compiled from the literature encompassing the efficacy of *L. formosana*. Its versatile  
59 utility as a medicine, food additive, nutraceutical, and ornamental function motivated us to  
60 bridge the information gap, and to form a comprehensive review on the chemical  
61 constituents identified from this plant and their divergent pharmacological properties.

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## 63 2. CHEMICAL CONSTITUENTS

64

### 65 2.1 Trace Elements

66 *L. formosana* are rich in essential trace elements. The contents of magnesium (Mg),  
67 manganese (Mn), and calcium (Ca) in wild *L. formosana* leaves are very high compared to  
68 black rice, black beans and black sesame seeds, nearly 3 times higher for Mg, 13 times  
69 higher for Mn, and 115 to 400 times higher for Ca, but its contents of Zinc (Zn) and copper  
70 (Cu) are the same compared to these black nutritious food [4, 5]. The leaf is the highest  
71 nutrient element in different organs, while the trunk had the lowest [6]. Therefore, *L.*  
72 *formosana* leaves can be used as medicinal plants and trace elements in food additives.  
73 Moreover, *L. formosana* have a strong enrichment capability for Cu, Zn, Mn, rare earth  
74 elements and other ions in soil [7], which are the material basis of blood glucose and blood  
75 pressure in medicinal values.

76

### 77 2.2 Volatile oils

78 *L. formosana* contains a large number of volatile oils that can be obtained from the leaf and  
79 fruit of this plant by steam distillation. Its typical essential oil constituents, such as terpenes,  
80 cinnamic acids and small amounts of monoterpenes ingredients, including  $\alpha$ -pinene,  $\beta$ -  
81 pinene, 4-terpineol,  $\alpha$ -terpineol, camphene, juniperene, terpinene (including  $\alpha$ ,  $\beta$ ,  $\gamma$ -  
82 configuration) are present [8, 9]. Sesquiterpene ingredients including vitispirane, valerenal,  
valerenone are also found.

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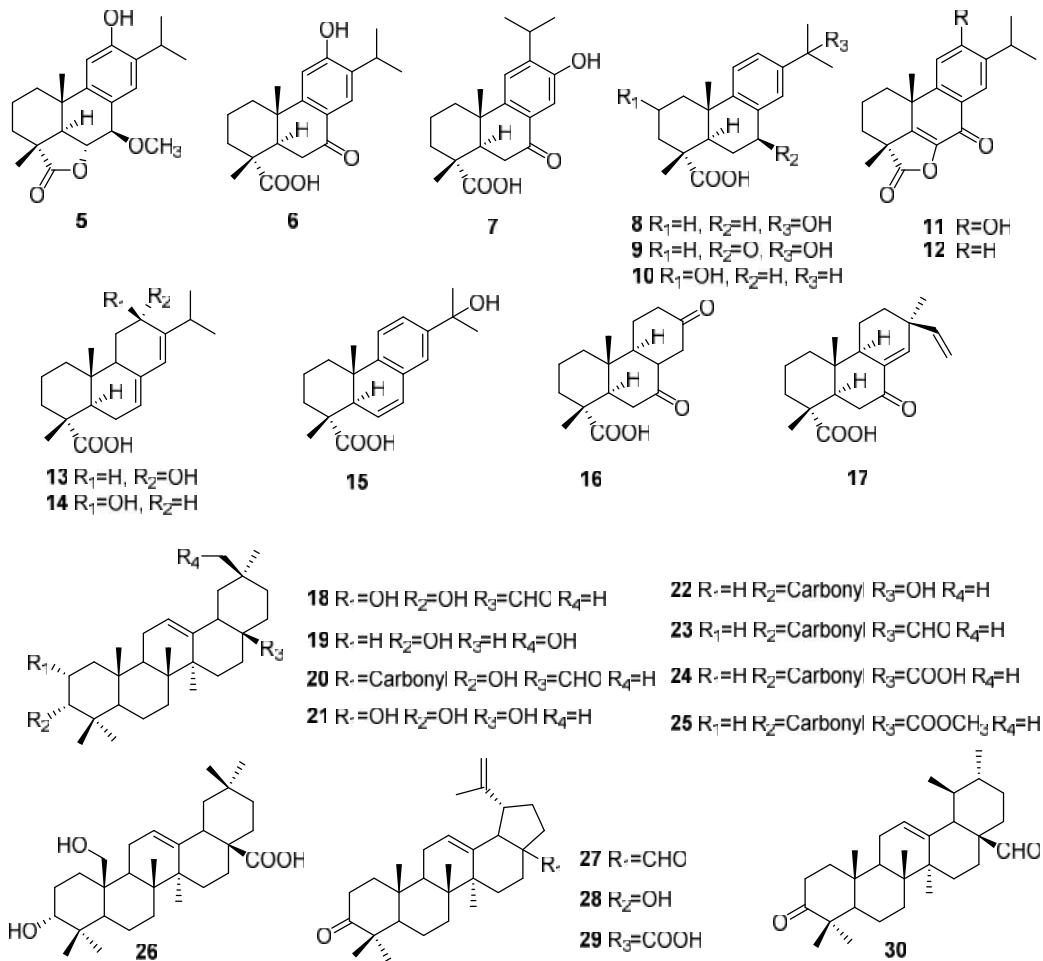
84 So far numerous studies have been conducted on different parts of *L. formosana* (Table 1).  
85 Remarkable differences are found in the main components and the relative contents of the  
86 essential oils among the different studied organs, indicating that the pharmacological effects  
87 of the various parts have significant differences. Moreover, volatile oil component of *L.*  
88 *formosana* and *L. styraciflua* indicates a closer relationship based on GC/MS methods of  
89 qualitative and quantitative analysis, but the genetic relationship between *L. storax* [10].  
90 Thus, leaves and resins from *L. formosana* were proved the potential sources for volatile oil.  
91 Differences of various organs, regional and species are the key factors in research and  
development of volatile oil.

92

### 93 2.3 Terpenoids

94 Terpenoids are the main chemical composition of *L. formosana*. A variety of compounds  
95 have been extracted and purified from the barks, resin of *L. formosana*, including diterpenes  
96 (such as iridoid and its derivatives) and triterpenoids (Table 2). The barks contain four iridoid  
glycosides (compounds 1-4), which was often regarded as important active ingredients in

97 medicinal plants [11]. A recent report showed that thirteen diterpenes (compounds 5-17)  
 98 were isolated from *L. formosana* resin [12]. Typical structures of triterpenoids, also contains  
 99 a range of normal tetracyclic (dammarane, tirucallane) and pentacyclic (lupane, oleanane)  
 100 triterpenoids are the most abundant components widely dispersed various organs of *L.*  
 101 *formosana*. More than fifty triterpenes were isolated from different parts of *L. formosana*.



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103 **Fig. 2 Structures of selected diterpenes and triterpenoids from *L. formosana***

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**Table 1. Analysis of volatile oils from different parts of *L. formosana***

Organs	Methods	Constituents	References
1 Leaf	GC/MS/DS	Twenty compounds were identified, accounting for 84.88%. 4-terpineol (27.17%), $\Delta$ 1(2), 8-menthadiene (9.39%), $\beta$ -caryophyllene (7.06%) and 7-hydroxycoumarin (6.82%) are the main ingredient.	[13]
2 Leaf	GC/MS	Forty-seven compounds were identified, accounting for 98.11% of naphtha, including 30 terpenoids, 14 aliphatic compounds and 3 aromatic compounds. The main components are $\beta$ -pinene (21.18%), $\alpha$ -pinene (20.70%), and (E)-2-hexenal (7.64%), limonene (7.59%), $\beta$ -caryophyllene (6.08%) , etc.	[14]
3 Leaf	GC/MS	Twenty-nine compounds were identified, accounting for 81.04% of the total essential oil. The main components are <i>n</i> -palmitic acid (27.03%) and 9,12,15-shap acid (13.35%).	[15]
4 Fruit	GC/MS	Twenty-nine compounds were identified. The main components compose of $\beta$ -pinene (16.69%), 1S- $\alpha$ -pinene (15.22%) and caryophyllene (12.54%).	[16]
5 Leaf	GC/MS	25 compounds were identified, accounting for 92.81% of total volatile oil, which contains 18 terpenes, 5 fatty substance and 2 aromatic substances. The main components were composed of $\alpha$ -pinene (34.48%), $\beta$ -pinene (19.25%), and limonene (26.97%).	[17]
6 Leaf, bark, heartwoo d	GC/MS	Fifteen components were identified from leaf, seven components from the bark, and nine components from heartwood.	[18]
7 Resin	GC/MS	Volatile oil in resin is 12%. The main components are $\alpha$ -pinene (24.92%), $\beta$ -pinene (23.62%), camphene (8.79%), terpinolene (6.41%), bornyl acetate (2.97%) and $\beta$ -caryophyllene (19.62). The content of caryophyllene is nearly 20%.	[19]
8 Resin	GC/MS	$\alpha$ -pinene (23.3%), $\beta$ -caryophyllene (22.7%) and $\beta$ -pinene (19.6%) are the main ingredient.	[20]
9 Leaf and stem	GLC/FID and GLC/MS	Sixty-four components were identified from the leaves and stems. The major components of the leaf were d-limonene (22.34%), $\alpha$ -pinene (27.95%) and $\beta$ -pinene (11.20%), and that of the stem oil were germacrene D (10.91%), $\alpha$ -cadinol, d-limonene (12.89%), $\alpha$ -pinene (14.19%), and $\beta$ -pinene (5.34%).	[1]

**Table 2 The reported terpenoids isolated from *L. formosana***

Sources	Compounds	References
Barks	monotropein (1)	[11]
	monotropein methyl ester (2)	
	6 $\alpha$ -hydroxy geniposidic (3)	
	6 $\beta$ -hydroxy geniposidic (4)	
Resin or balsam	liquidambolide A (5)	[12]
	liquiditerpenoic acid A (6)	
	liquiditerpenoic acid B (7)	
	15-hydroxydehydroabietic acid (8)	
	15-hydroxy-7-oxodehydroabietic acid (9)	
	2 $\alpha$ -hydroxydehydroabietic acid (10)	
	12-hydroxy-7-oxo-5,8,11,13-tetraene-18,6-abietanolide (11)	
	picealactone A (12)	
	12 $\alpha$ -hydroxyabietic acid (13)	
	12 $\beta$ -hydroxyabietic acid (14)	
	15-hydroxy-6-enedehydroabietic acid (15)	
	aguilarabietic acid K (16)	
	pimaric acid (17)	
	2 $\alpha$ ,3 $\alpha$ -dihydroxyolean-12-en-28-al (18)	[20]
	3 $\alpha$ -hydroxyolean-12-en-30-ol (19)	
	3 $\alpha$ -hydroxyolean-2-oxo-12-en-28-al (20)	
	3 $\alpha$ ,28-dihydroxyolean-12-ene (21)	
	28-hydroxy- $\beta$ -amyrone (22)	
	oleanonic aldehyde (23)	
	3-oxoolean-12-en-28-oic acid (24)	
	3-oxoolean-12-en-28-yl acetate (25)	
	3 $\alpha$ ,25-dihydroxyolean-12-en-28-oic acid (26)	
	3,28-dioxobetulin (27)	
	3-oxobetulin (28)	
	betulonic acid (29)	
	3-oxoursa-12-en-28-al (30)	
	liquidambronic acid (31)	[21]

	hmbronic acid (32) ambronic acid (33) formosolic acid (34) ambradiolic acid (35) liquidambronal (36) ambronal (37) oleanolic ketone alcohol (38) 3-oxo-olean-12-ene-28-oic acid (oleanonic acid) (39) 3-oxo-lup-20(29)-ene-28-oic acid (liquidambronic acid) (40)	[19]
Leaves	3 $\beta$ ,23,29-trihydroxy-olean-12-en-28-oic acid- $\beta$ -D-glucopyranosyl ester (41)	[22]
Roots	3 $\beta$ ,6 $\beta$ -dihydroxylup-20(29)-en-28-oic acid- $\beta$ -glucopyranosyl ester (42) 2 $\alpha$ -acetoxyl-3 $\beta$ ,6 $\beta$ -dihydroxylup-20(29)-en-28-oic acid- $\beta$ -glucopyranosyl ester (43) stigmast-4-en-3-one (44) (24R)-3 $\beta$ -hydroxy-24-ethylcholest-5-en-one (45) $\beta$ -amyrin (46) oleanonic acid (39) arjunic acid (47) hederagenin 28-O- $\beta$ -D-glucopyranoside (48) (2 $\alpha$ ,3 $\beta$ ,4 $\alpha$ )-23-(acetoxy)-2,3-dihydroxy-olean-12-en-28-oic acid- $\beta$ -D-glucopyranosyl arjunglucoside II (50) quadranoisde I (51) 2,4,6-trimethoxyphenol-1-O- $\beta$ -D-glucopyranoside (52) 3,30-di-O-methylellagic acid-40-O- $\beta$ -dxylopyranoside (53) 3,4,5-trimethoxyphenyl-(6-O-galloyl)-O- $\beta$ -D-glucopyranoside (54) 3,4,5-trimethoxyphenyl-6-O-syringoyl- $\beta$ -D-glucopyranoside (55)	[23]
Fruits	3-oxo-11 $\alpha$ ,12 $\alpha$ -epoxyoleanan-28, 13 $\beta$ -olide (56) 3-oxo-12 $\alpha$ -hydroxy-oleanan-28, 13 $\beta$ -olide (57) 3 $\alpha$ -acetoxyl-25-hydroxyoleanan-12-en-28-oic acid (58) oleanonic acid (39) ursolic acid (59) 2 $\alpha$ ,3 $\beta$ ,23-trihydroxyolean-12(13)-en-28-oic acid (arjunolic acid) (60) 2 $\alpha$ ,3 $\beta$ -dihydroxy-23-norolean-4(24),12(13)-dien-28-oic acid (61) 11 $\alpha$ -methoxyl-28-nor- $\beta$ -amyrone (62) 28-nor- $\beta$ -amyrone (63)	[24] [25] [26]

3-oxo-12 $\alpha$ -hydroxy-oleanan-28, 13 $\beta$ -olide ( <b>64</b> )
3 $\alpha$ -acetoxy-25-hydroxy-olean-12-en-28-oic acid ( <b>65</b> )
erythodiol ( <b>66</b> )
betulonic acid ( <b>67</b> )
styrcin ( <b>68</b> )

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3

## 4 2.4 Phenylpropanoids

5 Three phenylpropanoids, that is cinnamic acid cinnamic ester (69) [19], bornyl cinnamate (70), cinnamyl cinnamate (71) [20], were isolated and identified from *L. formosana* resin. The composition of the phenylpropanoids of *L. formosana* leaf 6 mainly consists of gallic acid (72), p-hydroxy-benzoic acid (73), 3-methoxy-4-hydroxy-benzoic acid (74), 3,5-dihydroxy-4- 7 methoxy-benzoic acid (75), 3,4-dihydroxy-benzoic acid (76), and 3,4-dihydroxy-5-methoxy-benzoic acid (77) [22]. Gallic 8 acid has good biological activity widely distributed in plants and foods [27], it was often being used to evaluate the quality 9 of this herb for its considerable contents in leaves and fruits of *L. formosana* [28].

## 10 11 2.5 Flavonoids

12 Flavonols and dihydro flavonols are the main existence forms of flavonoids in *L. formosana*. Several flavonoids, such as 13 rutin (78), isoquercitrin (79), hyperin (80), trefoil bean glycosides (81), astragalin (82), catechins (83), epigallocatechin (84) 14 were obtained from *L. formosana* (Figure 3). In recent years, (2S)-5,7,4'-trihydroxyflavan-7-O- $\beta$ -D-glucopyranoside (85), 15 (2S)-5,7,4'-trihydroxy-5-O- $\beta$ -D-glucopyranoside (86) and other new flavan glycosides were found in *L. formosana* leaf 16 [29]. Flavonoids are also used as a class of common pigments with good antioxidant activity widely used in industry. The 17 impact of various factors on total flavonoids extraction rate was determined for optimum extraction technology of total 18 flavonoids [30]. Moreover, dynamic changes of flavonoids content were measured in different leaf during various 19 collection periods. The optimal harvest time of *L. formosana* leaves were determined based on the contents of flavonoids 20 with different collection time [31]. Our study found that mature leaves as flavonoid-rich additives are the best resources of 21 natural food pigments for the extraction in food technology [32].

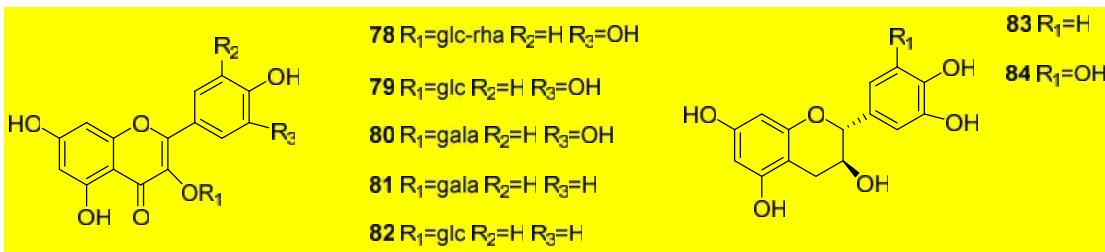


Fig. 3 Structures of selected flavonoids from *L. formosana*

## 2.6 Tannins and other compounds

Tannins are one of the main components in leaves, branches, and barks of *L. formosana*. Tannin content in leaf is nearly 13%, much higher than that of the bark [33], whereas *L. formosana* branch has the lowest concentration level of tannin [34]. Furthermore, the leaf has been reported to contain a fairly unique group of constituents called pigments, namely red pigment and melanin [35-37], which were commonly used as safe additives in food industry. (7S,8S)-3-methoxyl-3'-O- $\beta$ -D-glucopyranosyl-4':7,5':8-diepoxyneolignan-4,9'-diol [29], choline, acetylcholine, glucuronidase,  $\beta$ -sitosterol,  $\beta$ -sitosterol glucoside, 5-formylbilinone have also been isolated from the leaf of *L. formosana*.

## 3. PHARMACOLOGICAL ACTIVITIES

### 3.1 Antitumor and anticancer

Petroleum ether and dichloromethane extracts of Lulutong exhibited significantly cytotoxic on human colon adenocarcinoma cells HT-29, whereas methanol extract showed a minimal to negligible effect on cytotoxicity [38]. It has been found that 25-acetyl-3 $\alpha$ -hydroxy oleanolic 12-en-28-oic acid and 3 $\alpha$ , 25-dihydroxy-12-ene oleanolic acid, two triterpenic acid isolated from Lulutong showed significant inhibitory effects on HT-29 and HCT-116 cells. Another two oleanane triterpenoid acids, 3 $\alpha$ -acetoxy-25-hydroxy-olean-12-en-28-oic acid and lantanolic acid isolated from the MeOH extract of the fruit by activity-guided fractionation, had not been reported as NFAT transcription factor regulators. These compounds were proven to be a potent antitumor promoting activity using an in vitro assay on NFAT with IC<sub>50</sub> of 4.63  $\mu$ M (3 $\alpha$ -acetoxy-25-hydroxy-olean-12-en-28-oic acid) and 12.62  $\mu$ M (lantanolic acid), respectively [39]. On the other hand, among these pentacyclic triterpenes, oleane triterpenes with 3-keto skeleton showed significantly cytotoxicity against MDA-MB-435S tumor cells [40], suggesting that the 3-keto group is a critical structural factor for activity. The result indicated that triterpenic acids are a class of important anti-tumor components widely distributed in this plant.

### 3.2 Antithrombotic activity

The extracts of *L. formosana* resin and volatile oil at the dose of 1.0 mg/mL can obviously inhibit thrombus formation in all treated animals. Its antithrombotic effect was related to promoting plasmin activity and increase the level of cAMP on platelet, indicating the extracts of *L. formosana* resin had antithrombotic effect [41]. The recalcification experiment shows that volatile oil from leaves has also a good coagulation effect in vitro [42]. 28-oleanolic acid type carboxyl triterpenoids compounds from the extracts of maple and petroleum ether significantly inhibited ADP-induced platelet aggregation, suggesting that pentacyclic triterpenoids have anti-platelet aggregation activity [40].

### 53 3.3 Antimicrobial and antiviral activities

54 The extracts of *L. formosana* leaves are commonly used as an antibacterial material in traditional folk medicine in China.  
55 In vitro antibacterial activity, *L. formosana* leaves showed strong effects against *Staphylococcus aureus*, *Staphylococcus*,  
56 *Shigella flexneri*, typhoid common pathogens and opportunistic pathogens. However, little inhibition effects were found on  
57 *Escherichia coli* and *Candida albicans* [43]. Essential oil from *L. formosana* leaves have also a good stability in the acidic  
58 environment, which shows strong inhibition of gram-positive bacteria and fungi, such as *Bacillus subtilis*, *Staphylococcus*  
59 *aureus*, *Escherichia coli*, *Aspergillus flavus* and *Penicillium*, but relatively weak against Gram-negative bacteria [44].  
60 Several compounds, such as 3 $\alpha$ ,25-dihydroxy-12-en-28-oic acid and bornyl cinnamic acid from the essential oils of *L.*  
61 *formosana*, were found to be responsible for the antibacterial effects on *Lenzites betulina* and *Laetiporus sulphureus* [20].

62 A recent report showed that the extract of *L. formosana* may be applicable as an inhibitor of Neuraminidase (NA, as  
63 sialidase influenza virus) on influenza virus A/California/7/2009 (H1N1) NYMCNA test in vitro [45]. It can reduce the  
64 replication of the virus, and reduce cytopathic effect (CPE) and the amount of virus induced by the MDCK cells when the  
65 concentration of the extract was at the dose of 25-250  $\mu$ g/mL.

### 66 3.4 Anti-inflammatory activity

67 Activated NFAT can promote the migration and invasion of cancer cells. However, excessive activated NFAT will cause a  
68 series of pathological and inflammatory reactions, such as autoimmunity and immune rejection. Dat et al [39] found that  
69 oleanane-type triterpenoids from the methanol extract of Lulutong have strong inhibitory activity of NFAT. An aqueous  
70 decoction of Lulutong has anti-inflammatory and analgesic effects to the rat's paw edema induced by yeast. Furthermore,  
71 the essential oil obtained from *L. formosana* leaf was also demonstrated to exhibit anti-inflammatory activity in BEAS-2B  
72 human lung by detecting the expression of IL-6 protein used dexamethasone + TNF- $\alpha$ -induced cells as a positive control  
73 group (Dex) in epithelial cell inflammation model [42]. The underlying mechanisms for anti-inflammatory activity include  
74 reducing nitrite oxide generation, secretion levels of TNF- $\alpha$  and IL-6, and expression levels of prointerleukin- $\beta$ , inducible  
75 nitric oxide synthase, and cyclooxygenase-2 in lipopolysaccharide (LPS)-activated mouse macrophages [9].

### 76 3.5 Antidepressant activity

77 Monoamine oxidase (MAO) is a flavin adenine dinucleotide (FAD), containing enzyme of the outer mitochondrial  
78 membrane. The organic acid extracts of *L. formosana* showed strong inhibition activity to MAO with inhibition at  $IC_{50} < 10$   
79  $\mu$ g/mL, suggesting good antidepressant activity of *L. formosana* [46]. It was also found that the total phenolic extracts of  
80 the fruits of *L. formosana* strongly inhibited MAO with an  $IC_{50}$  value of 5.9  $\mu$ g/mL. Further bioactivity-guided  
81 chromatographic fractionation led to the isolation of gallic acid, ethyl gallate, p-digalloyl acid, and ethyl-p-digallate. These  
82 compounds showed high inhibitory activities in vitro against rat liver MAO with  $IC_{50}$  values of 1.7, 1.9, 1.5, and 1.1  $\mu$ g/mL,  
83 respectively, whereas the standard  $IC_{50}$  value of iproniazid was 1.8  $\mu$ g/mL [47]. So, the fruits of *L. formosana* can be used  
84 as anti-depressant drugs levy.

### 85 3.6 Antioxidant activity

86 *L. formosana* has been reported to exhibit other diverse activities, such as antioxidant activity. The extracts of *L.*  
87 *formosana* leaf showed good antioxidant activities than butylated hydroxytoluene (BHT), a synthetic antioxidant. The order  
88 of leaf extract with oxidation resistance is ethanol extracts > aqueous extract > acetone extract [48]. A methanol extract of  
89 *L. formosana* fruits also exhibited strong antioxidant activity, whereas petroleum ether and dichloromethane fractions had  
90 minimal or negligible effects [38].

91 Furthermore, the extract of *L. formosana* leaf can significantly improve the phagocytic percentage and phagocytic index of  
92 peritoneal macrophages in mice, suggesting a good enhanced non-specific immunity and cellular immunity effect [49].

## 93 4. FUTURE PROSPECTS

94 *L. formosana* is regarded as an important medicinal and ornamental plant with various economic, medicinal and  
95 ornamental benefits and ecological potential. Although preliminary studies of *L. formosana* are under way in different  
96 laboratories to use the antitumor, antithrombotic, antiinflammatory, antimicrobial, antiviral and antidepressant activities,  
97 these studies should be extended to humans in view of the medicinal nature of the plant. Moreover, diverse  
98 pharmacological activities of *L. formosana* are attributed to phytochemical compositions, especially volatile oils,  
99 phenylpropanoids, flavonoids and terpenoids rich in leaves, resins, and fruits, which are responsible for the effects of this  
100 medicinal plant. Most of the terpenoids identified in this paper were obtained from the extracts of resins, roots and fruits.  
101 Most of the flavonoids were found from the leaves. Phenylpropanoids exist widely in various parts of *L. formosana*.  
102 Terpenoids, flavonoids and phenylpropanoids as three kinds of main active constituents are also widely used as reference  
103 to determine medicinal plants quality.

106 Food additives obtained from natural product have become the most important way for humans to enrich food resource. *L. formosana*, known to contain trace elements, pigments, phenylpropanoids, and flavonoids with noteworthy antioxidant  
107 activity, may be a good candidate as food additives. However, the volatile oils composition of *L. formosana* is strongly  
108 influenced by both different parts and geographical origins factors, which were determined by GC-MS.  
109

110 As a folk medicine, different parts of *L. formosana* have its medicinal values. Resin and fruits as two important TCMs  
111 recorded in "Chinese Pharmacopoeia" attract more attentions than other organs. *L. formosana* resin is rich in essential  
112 oils and has been developed as a spice. It is noted that resin as a relatively scarce and expensive resource, should have  
113 further deeply research in terms of quality control and evaluation, such as identification between *L. formosana* resin and  
114 pine rosin.

115 In summary, although numerous studies have been conducted on different parts of *L. formosana*, but there is a dire need  
116 to be carried out in isolation and identification of new compounds from different parts of this plant in the near future. With a  
117 suitable pharmacological model, more studies will gradually screen the main active ingredients or the pure compounds  
118 from the crude extracts of *L. formosana*. Furthermore, these biologically active compounds can be determined  
119 quantitatively by HPLC analysis, which can be used to control the quantity of this plant. *L. formosana* will be further  
120 developed as medicinal and economic values, and thereby promote its cultivation.  
121

## 122 Ethical Approval

123 Not Applicable

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## 132 COMPETING INTERESTS

134 Authors have declared that no competing interests exist.  
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