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Chemical constituents and bioactivities of *Blumea balsamifera* (Sembung): a systematic review

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Abstract

Blumea balsamifera (Sembung) is a very famous ethnic medicinal herbs and functional tea in many countries of Asia. Phytochemical investigations showed that *B. balsamifera* contains various type chemical components, including volatile oil, flavonoids, terpenoids, phenylpropanoids, polysaccharides, etc. *B. balsamifera* has many pharmacological activities such as antioxidation, antibiosis, antitumor, liver protection, anti-inflammation, analgesia, and wound healing. This paper reviewed the chemical constituents and pharmacological activities of *B. balsamifera* for the further research, development, and utilization of *B. balsamifera.*

Keywords: *Blumea balsamifera*; phytochemical constituents; pharmacological activity.

Practical Application: The review provides a comprehensive information for consumers and researchers to understand Sembung Chemical constituents and bioactivities.

1 Introduction

Blumea balsamifera (L.) DC. is a very famous ethnic medicinal herbs and functional tea in many countries of Asia, such as China (named Ainaxiang), Malaysia (named Sembung), Philippines, Thailand, and Vietnam (Tan et al., 2020, 2023; Wang et al., 2023). The previous reports showed that *B. balsamifera* contains various type chemical components, including volatile oil, flavonoids, terpenoids, phenylpropanoids, polysaccharides, etc. and the chemical components of *B. balsamifera* have a variety of physiological activities, such as antioxidant, antibacterial, antifungal, anti-inflammatory, hypolipidemic, anti-infertility, liver protection, anti-diabetes, stomach protection, anti-tumor and so on (Tan et al., 2012; Widhiantara & Jawi, 2021).

The two main ingredients (L-Borneol and Blumea balsamiferae oleum) in *Blumea balsamifera* are the main components of many proprietary Chinese medicines such as Yinlishuang pills, Yankang tablets, Jinhoujian Spray, and Xinwei Zhitong Capsules. In addition, *B. balsamifera* is also widely used in the field of cosmetics based on its unique aromatic odor and burn treatment effect. This paper reviewed the chemical constituents and pharmacological activities of *B. balsamifera* for the further research, development, and utilization of *B. balsamifera.*

2 Chemical composition

There are more than 100 volatile or nonvolatile chemical components isolated from *B. balsamifera* (Chen et al., 2009; Pang et al., 2014a), including volatile oils, flavonoids, terpenoids, phenylpropanoids, steroids, etc., of which volatile oils, flavonoids, and sesquiterpenes are the most abundant and are the main chemical components of *B. balsamifera*, with a variety of in vitro and in vivo biological activities.

2.1 Essential oil

Essential oil is an important kind of chemical components with pharmacological activity in *B. balsamifera*. The main essential oil components include (-)-bromelain, trans-gastrolene, γ-eudesmol, α-eudesmol, anthocyanin, gastrolene oxide, and camphor (He et al., 2020; Yang et al., 2021). Although the categories of volatile components in *B. balsamifera* are similar due to the origin, harvesting time, and extraction method, there are some differences in the content of specific components (Yuan et al., 2016).

2.2 Flavonoids

Flavonoids are one of the more reported classes of components in *B. balsamifera* in recent years, and with a wide range of pharmacological activities have also greatly expanded the scope of clinical applications of *B. balsamifera* medicinal herbs(Pang et al., 2017). At present, scholars have isolated a total of 56 flavonoids from different parts of *B. balsamifera*, including dihydroflavonoids (compounds 1-8), dihydroflavonols

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(compounds 9-22), flavonoids (compounds 23-28), flavonols (compounds 29-50), chalcones (compounds 51, 52), paclitaxel (compounds 53, 54), and flavonoid dimers (compounds 55, 56). The names of these compounds are shown in Table 1, and their structures are shown in Figure 1.

In addition, in order to improve the production of flavonoid active ingredients in *B. balsamifera* in terms of biosynthesis, Xia et al. (2016) compared the transcriptome sequencing results of *B. balsamifera* with those of the biosynthetic pathways of flavonoids in other higher plants in the KEGG database and predicted that the metabolic pathway of flavonoids in *B. balsamifera*, and the key enzymes were CHS and chalcone isomerase, which provide a direction for further research on the biosynthesis of flavonoids in *B. balsamifera*.

2.3 Terpenoids

Terpenoids are a common class of compounds in *B. balsamifera*. Their cytoskeleton types include Monoterpenoids, sesquiterpenes, diterpenes, triterpenes and so on. Sesquiterpene lactone has attracted attention because of its cytotoxicity and potential antitumor activity. L-borneol, a famous traditional Chinese medicine, is a kind of bicyclic monoterpene, and its important plant source is *B. balsamifera*. At present, 5 sesquiterpenes, 51 sesquiterpenes and 5 diterpenes were isolated from *B. balsamifera*, and 2 ursolane triterpenes were isolated from the aboveground part of *B. balsamifera*. The name of the compound is shown in Table 2, and the chemical composition and structure are shown in Figure 2.

Table 1. Flavonoids isolated from *B. balsamifera* (1-56).

No.	Compound name	Formula	Molecular weight	Part of plant	Type	Ref.
1	Eriodictyol	$C_{15}H_{12}O_6$	288.26	Leaf	Dihydroflavonoids	(Zhao et al., 2007)
2	7-methyl-eriodictyol	$C_{16}H_{14}O_6$	302.28	Leaf		(Osaki et al., 2005)
3	Blumeatin	$C_{16}H_{14}O_6$	302.28	Aboveground part		(Chen et al., 2010b)
4	3',5,5',7-tetrahydroxyflavanone	$C_{15}H_{12}O_6$	288.26	Aboveground part		(Chen et al., 2010b)
5	Liquiritigenin	$C_{15}H_{12}O_4$	256.26	Leaf, Stem		(Huang et al., 2014)
6	Isohemiphloin	$C_{21}H_{22}O_{10}$	434.39	Aboveground part		(Zhou et al., 2021)
7	2',5,5',7-tetrahydroxyflavanone	$C_{15}H_{12}O_6$	288.26	Aboveground part		(Osaki et al., 2005)
8	3',4',5-trihydroxy-7-methoxyfavanone	$C_{16}H_{14}O_6$	302.28	Aboveground part		(Chen et al., 2009)
9	Blumeatin A	$C_{16}H_{14}O_7$	318.28	Leaf, Stem	Dihydroflavonols	(Zhao et al., 2007)
10	3,4',5-trihydroxy-3',7-dimethoxyflavanone	$C_{17}H_{16}O_7$	332.31	Leaf		(Chen et al., 2009)
11	3,3',5-trihydroxy-4',7-dimethoxyflavanone	$C_{17}H_{16}O_7$	332.31	Leaf		(Zhao et al., 2007)
12	3,3',4',5-tetrahydroxy-7-methoxyflavanone	$C_{16}H_{14}O_7$	318.28	Leaf		(Chen et al., 2009)
13	3,3',5,5',7-pentahydroxyflavanone	$C_{15}H_{12}O_7$	304.25	Leaf		(Gao et al., 2016)
14	2',3,5,7-tetrahydroxy-5'-methoxyflavanone	$C_{16}H_{14}O_7$	318.28	Aboveground part		(Osaki et al., 2005)
15	2',3,5-trihydroxy-5',7-dimethoxyflavanone	$C_{17}H_{16}O_7$	332.31	Aboveground part		(Chen et al., 2009)
16	(2R, 3R)-dihydroquercetin-4′-methyl ether	$C_{16}H_{14}O_7$	318.28	Leaf		(Chen et al., 2009)
17	Taxifolin	$C_{15}H_{12}O_7$	304.25	Leaf, Branch		(Hu et al., 2018)
18	(2R,3R)-dihydroquercetin-4',7-dimethyl ether	$C_{17}H_{16}O_7$	332.31	Leaf		(Chen et al., 2009)
19	(2R,3S)-(−)-4′-O-methyldihydroquercetin	$C_{16}H_{14}O_7$	318.28	Aboveground part		(Nguyen & Nguyen, 2012)
20	5,4'-dihydroxy-3,7,3'-trimethoxydihydroflavone	$C_{18}H_{18}O_7$	346.34	Leaf, Stem		(Huang et al., 2010)
21	5,7,3′,4′-tetrahydroxy-2-methoxy-3,4-flavandione 3-hydrate	$C_{16}H_{14}O_9$	350.28	Leaf, Branch		(Hanh et al., 2021)
22	Catechin	$C_{15}H_{14}O_6$	290.27	Leaf		(Chen et al., 2010a)
23	Luteolin	$C_{15}H_{10}O_6$	286.24	Leaf	Flavonoids	(Zhao et al., 2007)
24	Diosmetin	$C_{16}H_{12}O_6$	300.27	Leaf, Branch		(Yan et al., 2012)
25	Chrysoeriol	$C_{16}H_{12}O_6$	300.27	Leaf, Branch		(Yan et al., 2012)
26	Luteolin-7-methyl ether	$C_{16}H_{12}O_6$	300.27	Leaf		(Osaki et al., 2005)
27	Velutin	$C_{17}H_{14}O_6$	314.29	Leaf		(Osaki et al., 2005)
28	4',5-dihydroxy-7-methoxyflavone	$C_{16}H_{12}O_5$	284.27	Leaf, Stem		(Huang et al., 2010)

Table 1. Continued...

No.	Compound name	Formula	Molecular weight	Part of plant	Type	Ref.
29	Quercetin	$C_{15}H_{10}O_7$	302.24	Aboveground part	Flavonols	(Chen et al., 2010b; Nguyen & Nguyen, 2012)
30	Ombuin	$C_{17}H_{14}O_7$	330.29	Leaf		(Chen et al., 2009)
31	Tamarixetin	$C_{16}H_{12}O_7$	316.27	Leaf		(Cao et al., 2007; Hu et al., 2018; Saewan et al., 2011)
32	Rhamnetin	$C_{16}H_{12}O_7$	316.26	Leaf		(Chen et al., 2009)
33	3,5,7-trihydroxy-3',4'-dimethoxyflavone	$C_{17}H_{14}O_7$	330.29	Leaf, Branch		(Tan et al., 2012)
34	3,5-dihydroxy-3',4',7-trimethoxyflavone	$C_{18}H_{16}O_7$	344.32	Leaf, Branch		(Yan et al., 2012)
35	7,5′-Dimethoxy-3,5,2′-trihydroxyflavone	$C_{17}H_{14}O_7$	330.29	Aboveground part		
36	Chrysosplenol C	$C_{18}H_{16}O_8$	350.32	Leaf, Branch		(Yan et al., 2012)
37	Hyperoside	$C_{21}H_{20}O_{12}$	464.38	Leaf, Branch		(Tan et al., 2012)
38	Isoquercitrin	$C_{21}H_{20}O_{12}$	464.38	Leaf, Branch		(Tan et al., 2012)
39	Ayanin	$C_{18}H_{16}O_7$	344.32	Leaf		(Osaki et al., 2005)
40	Quercetin-3,7,3'-trimethyl ether	$C_{18}H_{16}O_7$	344.32	Leaf		(Osaki et al., 2005)
41	Kumatakenin	$C_{17}H_{14}O_6$	314.29	Leaf, Stem		(Huang et al., 2014)
42	Quercetin-3,7-dimethyl ether	$C_{17}H_{14}O_7$	330.29	Leaf		(Osaki et al., 2005; Yuan et al., 2018)
43	Quercetin-3,3', 4'-trimethyl ether	$C_{18}H_{16}O_7$	344.32	Aboveground part		(Chen et al., 2010a; Nguyen & Nguyen, 2012)
44	4',5,7-trihydroxy-3,3'-dimethoxyflavone	$C_{17}H_{14}O_7$	330.29	Leaf		(Hu et al., 2018; Tan et al., 2012)
45	Quercetin-3,4'-dimethyl ether	$C_{17}H_{14}O_7$	330.29	Leaf		(Osaki et al., 2005)
46	3',4',5,7-tetrahydroxy-3-methoxyflavone	$C_{16}H_{12}O_7$	316.26	Leaf, Branch		(Tan et al., 2012)
47	3',4',5-trihydroxy-3,7 -dimethoxyflavone	$C_{17}H_{14}O_7$	330.29	Leaf		(Bouktaib et al., 2002)
48	3,3',4',5-tetrahydroxy-7-methoxyflavone	$C_{16}H_{12}O_7$	316.27	Leaf		(Cao et al., 2007)
49	Isorhamnetin-3-O-β-D-galactopyranoside	$C_{22}H_{22}O_{12}$	478.41	Branch		(Zhang & Tan, 2007)
50	Rutin	$C_{27}H_{30}O_{16}$	610.52	Leaf		(Zhu et al., 2003)
51	Davidigenin	$C_{15}H_{14}O_4$	258.27	Aboveground part	Chalcones	(Chen et al., 2010b)
52	Davidioside	$C_{21}H_{24}O_9$	420.41	Aboveground part		(Chen et al., 2010b)
53	Glycyrol	$C_{21}H_{18}O_6$	366.36	Leaf, Stem	Paclitaxel	(Huang et al., 2014)
54	Isoglycyrol	$C_{21}H_{18}O_6$	366.36	Leaf, Stem		(Huang et al., 2014)
55	3-O-7″-biluteolin	$C_{30}H_{18}O_{12}$	570.46	Leaf	Flavonoid dimer	(Ali et al., 2005)
56	7,4′,4″-tri-O-methylamentoflavone	$C_{33}H_{24}O_{10}$	580.53	Aboveground part		(Tan et al., 2013)

2.4 Phenylpropanoids

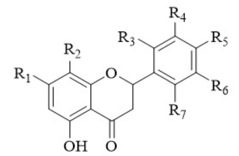
Fourteen common phenylpropanoids and one coumarin were isolated from *B. balsamifera*, among which the simple phenylpropanoids existed as esters or glycosides. Phenylpropanoids in *B. balsamifera* are shown in Table 3 and Figure 3.

2.5 Others

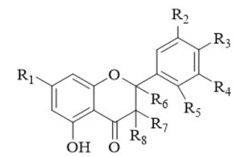
In addition to the above chemical components, it was found that *B. balsamifera* contains steroid compounds: β-sitosterol, stigmasterol, daucosterol, ergosterol peroxide, 4,22-stigmastadiene-3-one, 2-hydroxy-4,6-dimethoxyacetophenone, 2,4-dihydroxy-6-methoxyacetophenone, paraben, phytol, β-carotene, lutein, hentriacontane, et al (Table 4, Figure 4).

3 Pharmacological activities

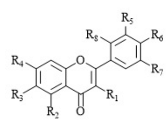
The previous pharmacological activity investigations on the whole plant of *B. balsamifera* and its crude extracts or chemical components found various pharmacological activities such as antioxidant, antibacterial, antitumor, hepatoprotective, anti-inflammatory, analgesic and wound healing promotion. Different chemical components show different pharmacological effects, such as: flavonoids play a certain role in antioxidation, antitumor, protect acute liver injury, promote blood aggregation and resist



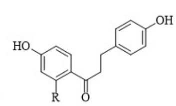
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
1	OH	H	H	H	OH	OH	H
2	OMe	H	H	H	OH	OH	H
3	OMe	H	H	OH	H	OH	H
4	OH	H	H	OH	H	OH	H
5	OH	H	H	H	OH	H	H
6	OH	Glu	H	H	OH	H	H
7	OH	H	OH	H	H	OH	H
8	OMe	H	H	OH	OH	H	H



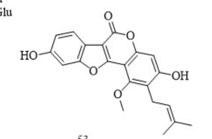
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
9	OH	H	OMe	OH	H	H	OH	H
10	OMe	H	OH	OMe	H	H	OH	H
11	OMe	H	OMe	OH	H	H	OH	H
12	OMe	H	OH	OH	H	H	OH	H
13	OH	OH	H	OH	H	H	OH	H
14	OH	OMe	H	H	OH	H	OH	H
15	OMe	OMe	H	H	OH	H	OH	H
16	OH	H	OMe	OH	H	H	OH	H
17	OH	H	OH	OH	H	H	OH	H
18	OMe	OH	OMe	H	H	H	OH	H
19	OH	H	OMe	OH	H	H	OH	H
20	OMe	H	OH	OMe	H	H	OMe	H
21	OH	H	OH	OH	H	OMe	OH	OH
22	OH	OH	OH	H	H	H	OH	H



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
23	H	OH	H	OH	H	OH	OH	H
24	H	OH	H	OH	H	OMe	OH	H
25	H	OH	H	OH	H	OH	OMe	H
26	H	OH	H	OMe	OH	OH	H	H
27	H	OH	H	OMe	OMe	OH	H	H
28	H	OH	H	OMe	H	OH	H	H
29	OH	OH	H	OMe	OH	OH	H	H
30	OH	OH	H	OMe	H	OMe	OH	H
31	OH	OH	H	OH	H	OMe	OH	H
32	OH	OH	H	OMe	H	OH	OH	H
33	OH	OH	H	OH	H	OMe	OMe	H
34	OH	OH	H	OMe	H	OMe	OMe	H
35	OH	OH	H	OMe	H	H	OMe	OH
36	OMe	OH	OH	OMe	H	OH	OMe	H
37	OGal	OH	H	OH	H	OH	OH	H
38	OGlc	OH	H	OH	H	OH	OH	H
39	OMe	OH	H	OMe	H	OMe	OH	H
40	OMe	OH	H	OMe	H	OH	OMe	H
41	OMe	OH	H	OMe	H	OH	H	H
42	OMe	OH	H	OMe	H	OH	OH	H
43	OMe	OH	H	OH	H	OMe	OMe	H
44	OMe	OH	H	OH	H	OH	OMe	H
45	OMe	OH	H	OH	H	OMe	OH	H
46	OMe	OH	H	OH	H	OH	OH	H
47	OMe	OH	H	OMe	H	OH	OH	H
48	OH	OH	H	OMe	H	OH	OH	H
49	OGal	OH	H	OH	H	OMe	OH	H
50	ORut	OH	H	OH	H	OH	OH	H



51 R=OH
52 R=OGlu



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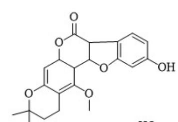

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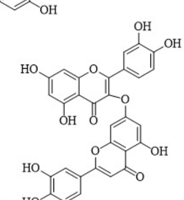

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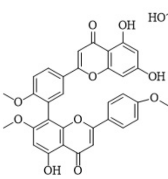

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Figure 1. Flavonoids isolated from *B. balsamifera*.

radiation. L-borneol and camphor in the volatile oil have good antibacterial, vasodilating and skin penetration promoting effects.

3.1 Antioxidant

Flavonoids and polyphenols are the main components of the antioxidant in *B. balsamifera* (Fazilatun et al., 2005; Pang et al., 2014c). Nguyen et al. (2004) investigated the effect of three crude extracts (methanol, methanol-water (1:1), and water) in inhibiting xanthine oxidase and found that among the three crude extracts, methanol extract was the most effective, methanol-water was the second most effective, and water was the least active. Nessa et al. (2004) further investigated the antioxidant aspects of the crude extracts of *B. balsamifera* and concluded that different crude extracts

Table 2. Terpenoids isolated from *B. balsamifera* (57-118).

No.	Compound name	Formula	Molecular weight	Part of plant	Type	Ref.
57	2,6-dimethyl-octa-1,7-diene-3,6-diol	$C_{10}H_{18}O_2$	170.25	Leaf	Monoterpenoids	(Xiong et al., 2022)
58	L-borneol	$C_{10}H_{18}O$	154.25	Leaf		(Wang et al., 2014)
59	Balsamiferoside B	$C_{16}H_{27}NaO_9S$	418.43	Leaf, Branch		(Hanh et al., 2021)
60	(1S,2R,4S)-borneol-β-D-glucopyranoside	$C_{16}H_{28}O_6$	316.39	Leaf, Branch		(Hanh et al., 2021)
61	(−)-angelicoidenol 2-O-β-D-glucopyranoside	$C_{16}H_{27}O_7$	331.38	Leaf, Branch		(Hanh et al., 2021)
62	2,3-dimethyloxiranecarboxylic acid (1R,3R,5E,10S)-10-hydroxy- 6,10- dimethyl -3- (1-methylethyl)-4,9-dioxocyclodec-5-en-1-yl ester	$C_{20}H_{30}O_6$	366.45	Leaf	Sesquiterpenes	(Osaki et al., 2005)
63	1,9-dihydroxy-4-eudesmen-6-one	$C_{15}H_{24}O_3$	252.35	Leaf		(Chen et al., 2009)
64	1-ang-4,7-dihydroxyeudesmane	$C_{20}H_{34}O_4$	338.49	Leaf		(Chen et al., 2009)
65	cryptomeridiol	$C_{15}H_{28}O_2$	240.39	Leaf		(Ragasa et al., 2005)
66	Blumealactones A	$C_{20}H_{28}O_6$	364.44	Leaf		(Chen et al., 2009)
67	Blumealactones B	$C_{20}H_{28}O_6$	364.44	Leaf		(Chen et al., 2009)
68	Blumealactones C	$C_{17}H_{24}O_6$	324.37	Leaf		(Chen et al., 2009)
69	2-methylbut-2-enoic acid(3aR,4S,5R,7R,8aS)-decahydro-3a,4-dihydroxy-4-methyl-7-(1-methylethyl)-1-methylidene-8-oxoazulen-5-yl ester	$C_{20}H_{30}O_5$	350.46	Leaf		(Osaki et al., 2005)
70	Blumeaene A	$C_{20}H_{30}O_5$	350.46	Aboveground part		(Chen et al., 2010b)
71	Blumeaene B	$C_{20}H_{30}O_5$	350.46	Aboveground part		(Chen et al., 2010b)
72	Blumeaene C	$C_{19}H_{30}O_5$	338.44	Aboveground part		(Chen et al., 2010b)
73	Blumeaene D	$C_{21}H_{32}O_5$	364.48	Aboveground part		(Chen et al., 2010b)
74	Blumeaene E	$C_{19}H_{28}O_6$	352.43	Aboveground part		(Chen et al., 2010b)
75	Blumeaene F	$C_{20}H_{30}O_6$	366.45	Aboveground part		(Chen et al., 2010b)
76	Blumeaene G	$C_{20}H_{30}O_5$	350.46	Aboveground part		(Chen et al., 2010b)
77	Blumeaene H	$C_{19}H_{30}O_5$	338.44	Aboveground part		(Chen et al., 2010b)
78	Blumeaene I	$C_{20}H_{30}O_6$	366.45	Aboveground part		(Chen et al., 2010b)
79	Blumeaene J	$C_{20}H_{32}O_7$	384.47	Aboveground part		(Chen et al., 2010b)
80	Blumpene B	$C_{20}H_{32}O_5$	352.47	Aboveground part		(Ma et al., 2018)
81	Blumpene C	$C_{19}H_{34}NO_5$	356.24	Aboveground part		(Ma et al., 2018)
82	Blumpene D	$C_{21}H_{33}O_5$	365.22	Aboveground part		(Ma et al., 2018)
83	Blumeaene E1	$C_{20}H_{30}O_6$	366.45	Leaf		(Shirota et al., 2011)
84	Blumeaene E2	$C_{20}H_{30}O_6$	366.45	Leaf		(Shirota et al., 2011)
85	Blumeaene K	$C_{20}H_{32}O_7$	384.47	Leaf		(Shirota et al., 2011)
86	Blumeaene L	$C_{17}H_{26}O_5$	310.39	Leaf		(Shirota et al., 2011)
87	Blumeaene M	$C_{20}H_{30}O_6$	366.45	Leaf		(Shirota et al., 2011)
88	Balsamiferine E	$C_{20}H_{32}O_5$	352.46	Aboveground part		(Xu et al., 2012)
89	Balsamiferine F	$C_{21}H_{32}O_5$	364.48	Aboveground part		(Xu et al., 2012)
90	Balsamiferine G	$C_{21}H_{32}O_5$	364.48	Aboveground part		(Xu et al., 2012)

Table 2. Continued...

No.	Compound name	Formula	Molecular weight	Part of plant	Type	Ref.
91	Balsamiferine H	$C_{15}H_{24}O_4$	268.35	Aboveground part	Sesquiterpenes	(Xu et al., 2012)
92	Balsamiferine I	$C_{20}H_{30}O_5$	350.45	Aboveground part		(Xu et al., 2012)
93	Balsamiferine J	$C_{20}H_{30}O_5$	350.45	Aboveground part		(Xu et al., 2012)
94	Balsamiferine N	$C_{20}H_{31}ClO_6$	402.91	Leaf		(Xiong et al., 2022)
95	Balsamiferine O	$C_{21}H_{34}O_7$	398.50	Leaf		(Xiong et al., 2022)
96	Blumeaene N	$C_{20}H_{30}O_6$	366.45	Leaf		(Yong et al., 2019)
97	Balsamiferine K	$C_{20}H_{32}O_7$	384.47	Leaf, Branch		(Hanh et al., 2021)
98	Inuchinenolide B	$C_{17}H_{22}O_5$	306.36	Leaf, Stem		(Huang et al., 2014)
99	Neogaillardin	$C_{17}H_{22}O_6$	322.36	Leaf, Stem		(Huang et al., 2014)
100	Cryptomeridiol	$C_{15}H_{28}O_2$	240.39	Leaf		(Ragasa et al., 2005)
101	Balsamiferine D	$C_{21}H_{36}O_3$	336.52	Aboveground part		(Ma et al., 2018)
102	Samboginone	$C_{15}H_{22}O_3$	250.34	Leaf		(Shirota et al., 2011)
103	Balsamiferine B	$C_{15}H_{22}O_3$	252.35	Aboveground part		(Xu et al., 2012)
104	Balsamiferine C	$C_{15}H_{22}O_3$	250.34	Aboveground part		(Xu et al., 2012)
105	1β,4β,7α-trihydroxyeudesmane	$C_{15}H_{28}O_3$	256.39	Leaf, Branch		(Hanh et al., 2021)
106	6,15α-epoxy-1β,4β-dihydroxyeudesmane	$C_{15}H_{26}O_3$	254.37	Leaf, Branch		(Hanh et al., 2021)
107	β-caryophyllene-8R,9R-oxide	$C_{15}H_{26}O$	220.36	Leaf		(Saifudin et al., 2012)
108	(4R,5R)-4,5-dihydroxycaryophyll-8(13)-ene	$C_{15}H_{26}O_2$	238.37	Aboveground part		(Ma et al., 2018)
109	Balsamiferine P	$C_{20}H_{28}O_5$	348.44	Leaf		(Xiong et al., 2022)
110	Balsamiferine Q	$C_{20}H_{28}O_5$	348.44	Leaf		(Xiong et al., 2022)
111	Balsamiferine R	$C_{20}H_{30}O_6$	366.45	Leaf		(Xiong et al., 2022)
112	Balsamiferine A	$C_{20}H_{29}ClO_5$	384.90	Aboveground part		(Xiong et al., 2022)
113	Blumpene A	$C_{20}H_{34}O_2$	306.49	Aboveground part	Diterpenoids	(Ma et al., 2018)
114	Sterebin P1	$C_{20}H_{34}O_4$	338.49	Aboveground part		(Ma et al., 2018)
115	Austroinulin	$C_{20}H_{34}O_3$	322.49	Leaf		(Xiong et al., 2022)
116	(7S,12Z)-12,14-labdadiene-7,8-diol	$C_{20}H_{34}O_2$	306.49	Aboveground part		(Ma et al., 2018)
117	Sterebin A	$C_{19}H_{32}O_3$	308.46	Leaf		(Pang et al., 2019)
118	Ursolic acid	$C_{30}H_{48}O_3$	456.71	Aboveground part	Triterpenes	(Zhou et al., 2021)
119	Ursolic acid lactone	$C_{30}H_{46}O_3$	454.70	Aboveground part		(Zhou et al., 2021)

of *B. balsamifera* have different degrees of antioxidant activity. Based on the above experimental results, Fazilatun Nessa inferred that the antioxidant activity of the flavonoids in *B. balsamifera* is mainly related to the number of hydroxyl groups, and the antioxidant activity of flavonoids containing one free hydroxyl group is greater than that of the methylated compounds (Fazilatun et al., 2005). In addition, Hu et al. (2018) found the strong antioxidant activity of flavonoids in *B. balsamifera* leaves by DPPH radical scavenging assay. Zhou et al. (2020) demonstrated that the antioxidant capacity was related to the presence of polyphenolic compounds by the effector surface method and Huihui & Jin (2013) found the strong antioxidant activity of essential oil of *B. balsamifera* leaves after DPPH radical scavenging assay, β-carotene bleaching assay and thiobarbituric acid assay. The above studies indicated that the essential oil of *B. balsamifera* has significant antioxidant activity and has the potential to be a natural antioxidant for food and cosmetics.

3.2 Antibacterial

Huihui & Jin (2013) confirmed that the essential oil had inhibitory activity against *Staphylococcus aureus*, *Aspergillus flavus*, *Candida albicans*, *Enterobacter*, *Salmonella*

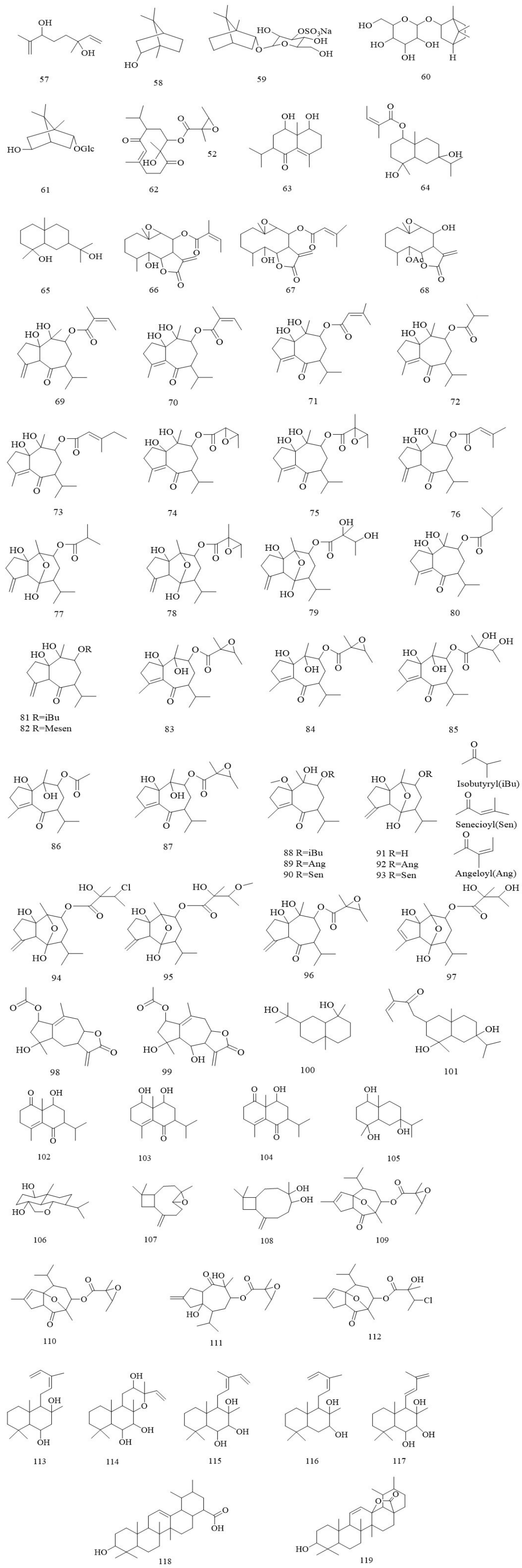

Figure 2. Terpenoids isolated from *B. balsamifera*.

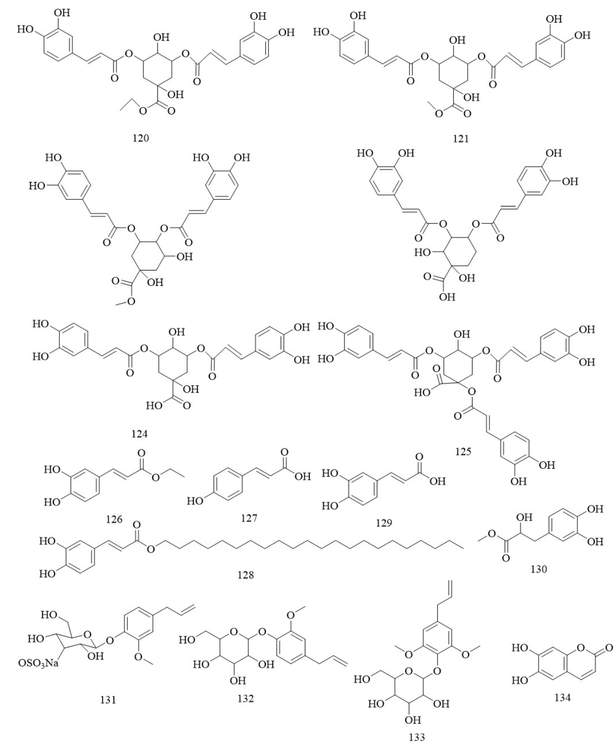

Figure 3. Phenylpropanoids isolated from *B. balsamifera*.

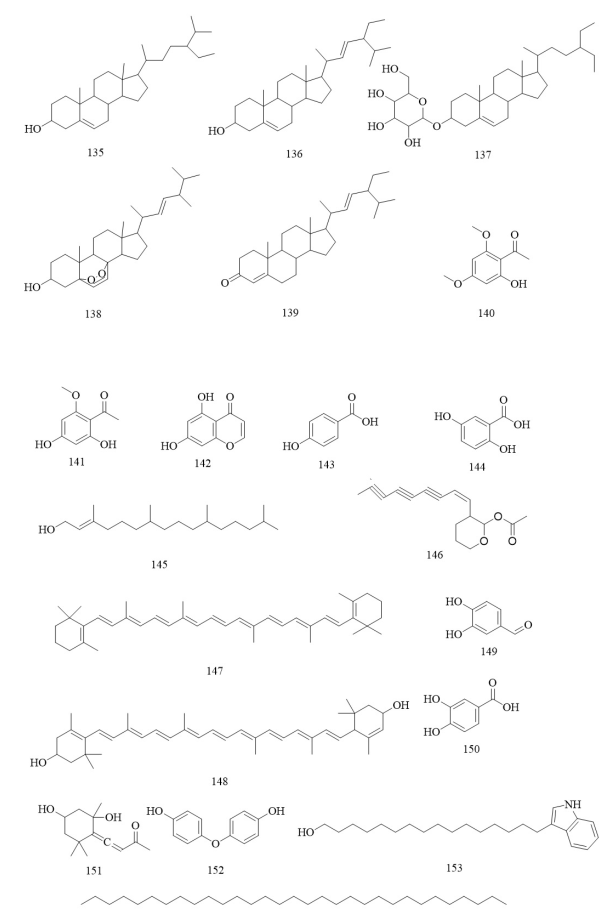

Figure 4. Other compounds isolated from *B. balsamifera*.

Table 3. Phenylpropanoids isolated from *B. balsamifera* (120-134).

No.	Compound name	Formula	Molecular weight	Part of plant	Ref.
120	3,5-*O*-dicaffeoylquinic acid ethyl ester	C27H28O12	545.10	Leaf	(Yuan et al., 2019)
121	3,5-*O*-dicaffeoylquinic acid methyl ester	C26H26O12	531.20	Leaf	(Yuan et al., 2019)
122	3,4-*O*-dicaffeoylquinic acid methyl ester	C26H26O12	531.20	Leaf	(Yuan et al., 2019)
123	3,4-O-dicaffeoylquinic acid	C25H24O12	515.11	Leaf	(Yuan et al., 2019)
124	3,5-*O*-dicaffeoylquinic acid	C25H24O12	515.11	Leaf	(Yuan et al., 2019)
125	1,3,5-tri-*O*-caffeoylquinic acid	C34H30O15	723.48	Leaf	(Yuan et al., 2019)
126	Ethyl caffeate	C11H12O4	208.21	Leaf	(Pang et al., 2019)
127	p-Hydroxycinnamic acid	C9H8O3	164.16	Leaf	(Pang et al., 2019)
128	Docosyl caffeate	C31H52O4	488.74	Leaf, Stem	(Huang et al., 2014)
129	Caffeic acid	C9H8O4	180.16	Leaf	(Yuan et al., 2018)
130	Methyl 3,4-dihydroxyphenyl lactate	C10H12O5	212.20	Aboveground part	(Zhou et al., 2021)
131	Balsamiferoside A	$C_{16}H_{21}NaO_{10}S$	428.38	Leaf, Branch	(Hanh et al., 2021)
132	Eugenyl-O-β-D-glucoside	C16H22O7	326.35	Leaf	(Pang et al., 2019)
133	4-allyl-2,6-dimethoxyphenol glucoside	C17H24O8	356.37	Leaf	(Pang et al., 2019)
134	6,7-dihydroxycoumarin	C9H6O4	178.14	Leaf	(Pang et al., 2019)

Table 4. Other compounds isolated from *B. balsamifera* (135-154).

No.	Compound name	Formula	Molecular weight	Part of plant	Ref.
135	β-Sitosterol	$C_{29}H_{50}O$	414.72	Leaf	(Chen et al., 2020; Zhao et al., 2007)
136	Stigmasterol	$C_{29}H_{48}O$	412.70	Leaf	(Zhao et al., 2007)
137	Daucosterol	$C_{35}H_{60}O_6$	576.86	Aboveground part	(Tan et al., 2013)
138	Ergosterol endoperoxide	$C_{28}H_{44}O_3$	428.66	Aboveground part	(Zhou et al., 2021)
139	4,22-Stigmastadiene-3-one	$C_{29}H_{46}O$	410.69	Leaf	(Zhang et al., 2015)
140	2-Hydroxy-4,6-dimethoxyacetophenone	$C_{10}H_{12}O_4$	196.20	Aboveground part	(Zhou et al., 2021)
141	2,4-Dihydroxy-6-methoxyacetophenone	$C_9H_{10}O_4$	182.18	Leaf, Branch	(Tan et al., 2012)
142	5,7-Dihydroxychromone	$C_9H_6O_4$	178.14	Leaf, Branch	(Tan et al., 2012)
143	Paraben	$C_7H_6O_3$	138.12	Aboveground part	(Tan et al., 2013)
144	2,5-dihydroxybenzoic acid	$C_7H_6O_4$	154.12	Aboveground part	(Tan et al., 2013)
145	phytol	$C_{20}H_{40}O$	296.54	Aboveground part	(Tan et al., 2013)
146	icthyothereol acetate	$C_{16}H_{16}O_3$	256.30	Leaf	(Ragasa et al., 2005)
147	β-Carotene	$C_{40}H_{56}$	356.89	Leaf	(Ragasa et al., 2005)
148	Lutein	$C_{40}H_{56}O_2$	568.89	Leaf	(Ragasa et al., 2005)
149	Protocatechualdehyde	$C_7H_6O_3$	138.12	Leaf	(Pang et al., 2019)
150	Protocatechuic acid	$C_7H_6O_4$	154.12	Leaf	(Pang et al., 2019)
151	(4R)-4-(3-Oxo-1-buten-1-ylidene)-3α,5,5-trimethylcyclohexane-1α,3β-diol	$C_{13}H_{20}O_3$	224.30	Leaf	(Pang et al., 2019)
152	4-(4-hydroxyphenoxy)phenol	$C_{12}H_{10}O_3$	202.21	Leaf	(Saifudin et al., 2012)
153	3-(hydroxyecetyl)indole	$C_{24}H_{39}NO$	357.58	Leaf	(Pang et al., 2019)
154	Hentriacontane	$C_{31}H_{64}$	436.84	Leaf	(Zhang et al., 2015)

and *Listeria monocytogenes*. And related studies found that *B. balsamifera* extract and volatile oil have anti-bacterial and fungal effects: n-hexane extract has inhibitory effect on *Enterobacter cloacae* and *Staphylococcus aureus*, dichloromethane extract has an inhibitory effect on *Enterobacter cloacae*, while volatile oil has a strong inhibitory effect on *Bacillus cereus*, *Staphylococcus aureus* and *Candida albicans* (Sakee et al., 2011). Volatile oil can destroy the integrity of the *Staphylococcus aureus* cell membrane, change its cell membrane permeability, inhibit bacterial nucleic acid and protein synthesis, cause amino acid metabolism disorder, and affect the activity of various enzymes and substance transport (Yang et al., 2021). Wang et al. (2019) isolated 15 monomer compounds from ethyl acetate, mainly flavonoids, and evaluated their antibacterial activity. It was found that the antimicrobial activity of vanillin against *Staphylococcus aureus* was the strongest, and the minimum inhibitory concentration

(MIC) was 32 μg / mL. In addition, He et al. (2020) studied the in vitro bacteriostatic effect of essential oil on *Haemophilus parasuis* and evaluated the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the essential oil. Wen et al. (2015) found that the extract of *B. balsamifera* residue has good antibacterial activity in vitro, and its chloroform extract has a significant inhibitory effect on *Escherichia coli* and type B *Hemolytic streptococcus*. The above studies show that *B. balsamifera* extract has a certain inhibitory effect on several infectious and toxin-producing microorganisms and can be used to prevent and treat microbial diseases.

3.3 Antitumor

Toshio et al (Norikura et al., 2008a, b) found that methanolic extract of *B. balsamifera* (BME) inhibited the growth of rat and human hepatocellular carcinoma cells. In addition, BME reduced the levels of proliferation-inducing ligands that stimulate tumor cell growth, suggesting a potential therapeutic effect of BME in patients with hepatocellular carcinoma. Hu et al. (2018) used cervical cancer (HeLa), breast cancer (MCF-7), lung cancer (A549), gastric cancer (MGC-803), and colon cancer (COLO-205) cell lines as donor cell lines and screened the cytotoxic activity of two sesquiterpene lactones isolated and purified from *B. balsamifera* using MTT method. The results showed that both Blumeaene E and Blumeaene N have cytotoxic activity.

3.4 Hepatoprotective effect

Xu & Zhao (1998) investigated the protective effects of 5,3',5'-trihydroxy-7-methoxydihydroflavone (BF-I) and four compounds (BF-II, BF-III, BF-IV, BF-V) obtained by structural modification of BF-I on acute liver injury. The results demonstrated that all five compounds had significant protective effects against acute liver injury caused by CCl4, AAP and TAA in rats, with BF-II showing the strongest activity, followed by BF-I, and then BF-III, BF-IV and BF-V. Zhao & Xu (1997) conducted a study on the pharmacological activity of BF-I and its structural modifiers and found that dihydroflavonoids have a strong inhibitory effect on lipid peroxidation. Pu et al. (2000) further demonstrated the protective effect of five dihydroflavonoids against CCl_4 or cysteine-induced lipid peroxidation in hepatocytes.

3.5 Anti-inflammatory and analgesic

In vivo experiments showed that essential oil of *B. balsamifera* significantly inhibited xylene-induced auricular swelling in mice, reduced the number of twists in acetic acid-induced mice, decreased the content of prostaglandin E2 in the inflammatory tissue of dimethylamine-induced mouse ears, and enhanced the activity of superoxide dismutase in mouse serum (Ma et al., 2016; Yi et al., 2016). In vitro experiments showed that essential oil significantly improved the morphological changes of LPS-induced RAW264.7 macrophages and reduced apoptosis. In addition, essential oil significantly inhibited the expression of leukocyte differentiation antigen 14, Toll-like receptor 4, myeloid differentiation primary response gene 88, and NOD-like receptor thermoprotein structural domain-associated protein 3 inflammatory vesicles in the NFκB signaling pathway (Liao et al., 2021). Through a comparative study of the anti-inflammatory effects of *B. balsamifera* herbs from different origins in Guizhou, Li et al. (2018) found that all the herbs from different origins also had certain anti-acute and chronic inflammatory effects. Cai et al. (2021) found that linalool and trans-stilbene are important anti-inflammatory components of essential oil, both of which can inhibit the release and expression of cellular inflammatory factors and inflammatory mediators.

3.6 Promotion of wound healing

By exploring the healing effect of essential oil on a rat deep second-degree burn model, Fan et al. (2015) found that essential oil treatment significantly reduced the water content of burned rat tissues, shortened the crusting time, accelerated healing, and significantly increased the expression of growth factors in tissues. Pang et al. (2014b) found that diluted essential oil promoted capillary regeneration, blood circulation, collagen deposition, granulation tissue formation, epithelial deposition and wound contraction by observing the effect of essential oil of *B. balsamifera* on wound healing in mice. The mechanism of action may be related to the induction of neuropeptide substance P secretion and mesenchymal cell proliferation and differentiation. However, undiluted essential oil may lead to skin thickening and sclerosis, inhibition of collagen synthesis and delayed skin wound healing. total flavonoids of *B. balsamifera* also promote skin wound healing in rats and the mechanism of action is related to increased expression levels of vascular endothelial growth factor, transforming growth factor β and hydroxyproline content at different stages of healing (Pang et al., 2017).

3.7 Hypoglycemia

Yan et al. (2014) found that the aqueous solutionof *B. balsamifera* (BBW) after extraction of volatile oil and ethyl acetate extract (BBE) of the alcoholic extract of the pomace after extraction of volatile oil had an inhibitory effect on α-glucosidase. Hu et al. (2018) obtained nine flavonoids from the leaves of *B. balsamifera*, 5 of which showed inhibitory effects on α-glucosidase. In addition, the aqueous and methanolic extracts of *B. balsamifera* also inhibited protein tyrosine phosphatase 1B with IC50 of 2.26 and 5.73 μg/mL, respectively (Saifudin et al., 2013, 2012).

3.8 Other pharmacological activities

Numerous studies have shown that *B. balsamifera* is an important medicinal plant, and pharmacological studies have focused on anti-microbial, anti-inflammatory effects, anti-tumor, wound healing, and anti-pathogenic activities, which confirm the traditional medicinal uses of the plant. In addition, several new pharmacological activities have been identified, such as antiviral (Xiong et al., 2022), anti-xanthine oxidase (Nguyen & Nguyen, 2012), and anti-obesity activities (Kubota et al., 2009).

4 Conclusion

In recent years, *B. balsamifera* has received more and more attention in many countries of Asia and extensive research has been conducted on its chemical constituents and pharmacological activities. Till now, 154 small molecular compounds including flavonoids, terpenoids, phenylpropanoids, steroids, etc. have been reported from *B. balsamifera*. The pharmacological investigations showed that B. balsamifera has various effects such as antioxidant, antibacterial, antitumor, hepatoprotective, anti-inflammatory, analgesic and wound healing promotion. This paper reviewed the chemical constituents and pharmacological activities of *B. balsamifera* for the further research, development, and utilization of *B. balsamifera.*

Conflict of interest

The authors declare no conflict of interest.

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