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Review

Ethnopharmacology, chemical composition and functions of *Cymbopogon citratus*

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ABSTRACT

Cymbopogon citratus in the gramineous family, also known as lemongrass (LG), is a perennial herb. LG, a drug and food homologous medicine, has a widely recorded medicinal value and food applications. To date, 158 LG compounds have been reported, including terpenoids, flavonoids, phenolic acids. Pharmacological and clinical studies have indicated that LG has antibacterial, neuroprotective, hypoglycemic, hypotensive, anti-inflammatory, and anti-tumor effects. This article reviews LG in ethnopharmacology, chemical composition, pharmacology, food, medicine, and daily chemical applications to provide a basis for the subsequent development of food and medicine.

Contents

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1. Introduction

The perennial herb *Cymbopogon citratus* (DC.) Stapf in the gramineous family is found throughout tropical and subtropical Asia and is cultivated in South Africa, other nations, and the southern provinces of China (Yang et al., 2020). The whole herb of *C. citratus* can be used as a traditional Chinese medicine called citronella, also known as lemongrass (LG), used in traditional Chinese medicine. LG, first recorded in the *Supplement to Materia Medica* (*Ben Cao Shi Yi* in Chinese) by Zangqi Chen (687–757) during the Tang Dynasty (AD 618–907) of China under the original name Xiangmao in Chinese, has now been included in *the Dictionary of Traditional Chinese Medicine* (*Zhongyao Da Cidian* in Chinese). LG is warm, pungent and sweet, and belongs to the lung, stomach and spleen meridians. LG has the effects of expelling wind unblocking collaterals, warming, and relieving pain, dampness and diarrhea. It often treats exogenous wind-cold headaches, rheumatic arthralgia, epigastric cold pain, diarrhea, edema, beriberi, and traumatic injuries (OuYang et al., 2016). Existing research has demonstrated that the main chemical components of LG are terpenoids, flavonoids, phenolic acids, and polysaccharides, which have antibacterial, neuroprotective, antidiabetic, anti-inflammatory, and other pharmacological activities (Umukoro, Ben-Azu, Ajayi, Adebesin, & Emokpae, 2020; Li et al., 2021). LG is commonly used to treat fever, diabetes and hypertension. LG has medicinal value and is used as a seasoning or tea substitute for food (Ekpenyong, Akpan, & Nyoh, 2015; OuYang et al., 2016; Dagupen et al., 2009). LG also has applications in daily chemicals and is often used to make soap, mouthwash. This study reviewed the ethnopharmacology, chemical composition, pharmacology, food, and clinical and daily chemical applications of LG by consulting recent literature to provide a basis for subsequent studies on the homology of medicine and food in LG.

2. Ethnopharmacology

LG has a long history of use as a seasoning in food and medicine to treat diseases in China and elsewhere. LG is frequently used in flavor food because of its distinctive scent. In Southeast Asian countries and China, many foods are often seasoned with LG, such as soup, berries, chicken, pork, and seafood dishes (Dagupen et al., 2009). In addition to food applications, LG is frequently brewed into tea to decrease blood pressure in Brazil, Cuba, and India (Carbajal, Casaco, Arruzazabala, Gonzalez, & Tolon, 1989; Moreira, Bastos, Blank, Alves, & Santos, 2010; Pereira, Marques, Sudo, Kaplan, & Zapata-Sudo, 2013). In Ayurveda, India's traditional treatment system, lemongrass essential oil (LGEO) treats hypertension, fever, stomach disease, and inflammation related to rheumatism, colds and flu (Khan & Ahmad, 2012). In addition, the LG leaf extract and decoction have various therapeutic effects, such as anti-inflammatory, cough-relieving, digestive, antiinfluenza, antipyretic, anti-diabetes and antimalarial (Bertea & Maffei, 2010). In tropical and subtropical countries, LG leaf infusion is widely used to regulate blood sugar, lipid, and fatty blood levels to prevent diabetes, hypertension, and obesity (Borges et al., 2021; Campos et al., 2014; Oladeji, Adelowo, Ayodele, & Odelade, 2019). In China, there are many folk records of the LG. LG, first recorded in the book *Supplement to Materia Medica* (*Ben Cao Shi Yi* in Chinese) published in 741 CE, has a warm, brilliant, and sweet taste. It disperses wind, clears collaterals, warms the middle, and relieves pain. It is commonly used to treat cold headaches, fever, abdominal pain, diabetes, hypertension, epilepsy, and anxiety. *The Lingnan Medication Collection* (*Ling Nan Cai Yao Lu* in Chinese) recorded that LG water decoction was used to treat headaches by washing the head, dispelling wind, reducing swelling by washing the body and avoiding fishy odors. The decoction was obtained by stir-fried LG and rice and then adding water to treat watery diarrhea. The abdominal pain was relieved using LGEO (Xiang, Wei, Xu, & Xiao, 2017). *The Sichuan Traditional Chinese Medicine Chronicle* (*Sichuan Zhong Yao Zhi* in Chinese) reported that bathing with 500 g LG of a water decoction could treat systemic pain caused by wind, cold and dampness. LG also has been recorded in *Guangdong Traditional Chinese Medicine* (*Guangdong Zhong Yao* in Chinese), *Guizhou Traditional Chinese Medicine* (*Guizhou Zhong Yao* in Chinese), and the *National Compilation of Traditional Chinese Medicine* (*Quan Guo Zhong Cao Yao Hui Bian* in Chinese), and has now been included in *Chinese Materia Medica* (*Zhonghua Bencao* in Chinese) (Editorial board of Chinese Materia Medica of National Administration of Traditional Chinese Medicine, 1999).

3. Chemical composition

LG has been extensively studied for its chemical components, including volatile oils, flavonoids, phenolic acids, phenylpropanoids, alcohols, esters, aldehydes and alkaloids. Volatile oils are a major component of LG, including monoterpenes, sesquiterpenes, and fewer diterpenes and triterpenes. The active monoterpenes identified were neral, geranial, geraniol, citronellal, and citronellol. At present, 158 chemical constituents of LG have been reported, of which 105 have been isolated and identified (**1**–**10**, **20**–**29**, **43**–**55**, **62**–**88**, **99**–**102**, **107**–**134**, **137**–**149**), and 48 have been analyzed by GC–MS (**11**–**19**, **30**–**42**, **56**–**61**, **89**–**98**, **103**–**106**, **135**, **136**, **150**–**153**).

3.1. Monoterpenes

Monoterpenes are composed of two isoprene units and contain 10 carbon atoms. Monoterpenes, widely distributed in the glands, oil chambers, resin ducts, and other secretory tissues of higher plants, are the significant components of volatile plant oils. A total of 61 monoterpenes were obtained from LG, including 21 acyclic monoterpenes (**1**–**21**), 22 monocyclic monoterpenes (**22**–**43**), and 18 bicyclic monoterpenes (**44**–**61**). Li et al. extracted the main components of LGEO from the aboveground part of LG, including citronellal (38.16%), geraniol (19.39%), and citronellol (17.18%), accounting for 75% of the total volatile oil (Li et al., 2021). Vanillin (45.2%) and total aldehyde (32.4%) were isolated from the main components of the essential oil by crushing and distilling LG leaves

(Koba et al., 2008). In summary, citronellal (**1**), geranial (**2**), neral (**5**), citronellol (**15**), and geraniol (**16**) were the primary monoterpene active ingredients of LG. Table 1 and Fig. 1 showed the monoterpenes in LG in detail.

3.2. Sesquiterpenes

Sesquiterpenes contain three isoprene units with chains, rings, and other skeletal structures. A total of 37 sesquiterpenes were obtained from LG, including one sesquiterpene chain (**62**) and 36 cyclic sesquiterpenes (**63**–**98**). β-Elemene (**96**) is an isomer of elemene, a lipid-soluble sesquiterpene, and an active component of LG with potential antineoplastic and chemopreventive activities. Sesquiterpenes from LG are shown in Table 2 and Fig. 2.

3.3. Diterpenes and triterpenes

Eight diterpenes and triterpenes were identified in LG. Diterpenes included two chains of diterpenes (**99** and **100**) and one cyclic diterpene (**101**). Five triterpenes (**102**–**106**) were cyclic. Carnosic

Table 1
Monoterpenes (**1**–**61**) isolated from LG.

No.	Molecular formulas	Compounds	References
1	$C_{10}H_{18}O$	Citronellal/β-Citronellal	Li et al., 2021
2	$C_{10}H_{16}O$	α-Citral/Citral/Geranial	Li et al., 2021
3	$C_{10}H_{16}O_2$	Geranic-acid/Neric acid	Ekpenyong, Akpan, & Nyoh, 2015
4	$C_{10}H_{18}O$	Nerol/*cis*-Geraniol	Ekpenyong, Akpan, & Nyoh, 2015
5	$C_{10}H_{16}O$	Neral/β-Citral/*cis*-Citral	Ekpenyong, Akpan, & Nyoh, 2015
6	$C_{10}H_{16}$	β-Myrcene/Myrcene	Ekpenyong, Akpan, & Nyoh, 2015
7	$C_{10}H_{16}$	β-Ocimene	Li et al., 2021
8	$C_{10}H_{18}O$	Linalool/*L*-linalool	Ekpenyong, Akpan, & Nyoh, 2015
9	$C_{10}H_{18}O$	(+)-Linalool/*D*-linalool	Kouame et al., 2015
10	$C_{10}H_{18}O$	Myrcenol	Ekpenyong, Akpan, & Nyoh, 2015
11	$C_{10}H_{16}$	(*E*)-β-Ocimene	Kpoviessi et al., 2014
12	$C_{10}H_{16}$	(*Z*)-β-Ocimene	Kpoviessi et al., 2014
13	$C_{10}H_{18}$	2,6-Octadiene, 2,6-dimethyl-	Li et al., 2021
14	$C_{10}H_{16}$	Artemisia triene	Li et al., 2021
15	$C_{10}H_{20}O$	Citronellol/β-Citronellol	Li et al., 2021
16	$C_{10}H_{18}O$	Geraniol	Li et al., 2021
17	$C_{10}H_{18}$	(-)-Citronellene	Li et al., 2021
18	$C_{10}H_{18}O$	Rose oxide	Li et al., 2021
19	$C_{10}H_{14}O_2$	Rosefuran epoxide	Li et al., 2021
20	$C_{10}H_{14}O$	Perillene	Yang et al., 2020
21	$C_{10}H_{18}O_2$	*cis*-Linaloloxide	Barbosa et al., 2008
22	$C_{10}H_{16}$	*D*-limonene	Li et al., 2021
23	$C_{10}H_{18}O$	α-Terpineol	Ekpenyong, Akpan, & Nyoh, 2015
24	$C_{10}H_{16}O$	*z*-Carveol	Kouame et al., 2015
25	$C_{10}H_{14}O$	Dextro-carvone	Ekpenyong, Akpan, & Nyoh, 2015
26	$C_{10}H_{16}O$	(-)-*trans*-Carveol	Ekpenyong, Akpan, & Nyoh, 2015
27	$C_{10}H_{18}O$	Terpinen-4-ol	Li et al., 2021
28	$C_{10}H_{18}O$	1,8-Cineole/Cineole/Eucalyptol	Li et al., 2021
29	$C_{10}H_{16}O$	α-Cyclocitral	Ekpenyong, Akpan, & Nyoh, 2015
30	$C_{10}H_{14}$	*O*-Cymene	Li et al., 2021
31	$C_{10}H_{14}$	*p*-Cymene	Kpoviessi et al., 2014
32	$C_{10}H_{16}$	β-Terpinene	Li et al., 2021
33	$C_{10}H_{16}$	γ-Terpinene	Li et al., 2021
34	$C_{10}H_{16}$	Terpinolene/α-Terpinolene	Li et al., 2021
35	$C_{10}H_{18}O$	*p*-Menthone/1-Menthone	Li et al., 2021
36	$C_{10}H_{18}O$	Isopulegol/*L*-isopulegol	Li et al., 2021
37	$C_{10}H_{20}O_2$	7-Hydroxymenthol	Zhang et al., 2014
38	$C_{10}H_{16}O$	*cis*-*p*-Mentha-2,8-dienol	Kpoviessi et al., 2014
39	$C_{10}H_{16}O$	α-Phellandren-8-ol	Kpoviessi et al., 2014
40	$C_{10}H_{18}O$	*L*-α-Terpineol	Li et al., 2021
41	$C_{10}H_{12}O$	Anethole	Li et al., 2021
42	$C_{10}H_{16}O$	*p*-Mentha-1(7),8(10)-dien-9-ol	Kpoviessi et al., 2014
43	$C_{10}H_{16}O$	*trans*-Chrysanthemal	Ekpenyong, Akpan, & Nyoh, 2015
44	$C_{10}H_{16}$	α-Pinene	Kouame et al., 2015
45	$C_{10}H_{16}$	Camphene	Kouame et al., 2015
46	$C_{10}H_{16}$	Tricyclene	Kouame et al., 2015
47	$C_{10}H_{14}O$	Verbenone	Kouame et al., 2015
48	$C_{10}H_{16}O$	Myrtenol	Yang et al., 2020
49	$C_{10}H_{16}O$	Myrtanal	Kouame et al., 2015
50	$C_{10}H_{18}O$	Borneol	Kouame et al., 2015
51	$C_{10}H_{16}O$	α-Pinene oxide	Ekpenyong, Akpan, & Nyoh, 2015
52	$C_{10}H_{16}O$	β-Pinene oxide	Ekpenyong, Akpan, & Nyoh, 2015
53	$C_{10}H_{16}O$	Sabinol	Kouame et al., 2015
54	$C_{10}H_{16}$	α-Thujene	Li et al., 2021
55	$C_{10}H_{16}$	3-Carene	Kouame et al., 2015
56	$C_{10}H_{16}O$	*trans*-3(10)-Caren-2-ol	Kpoviessi et al., 2014
57	$C_{10}H_{18}$	Pinane	Li et al., 2021
58	$C_{10}H_{16}$	β-Pinene	Kpoviessi et al., 2014
59	$C_{10}H_{16}$	1*R*-α-Pinene	Li et al., 2021
60	$C_{10}H_{18}$	Isocamphane	Li et al., 2021
61	$C_{10}H_{16}O$	*cis*-Verbenol	Kpoviessi et al., 2014

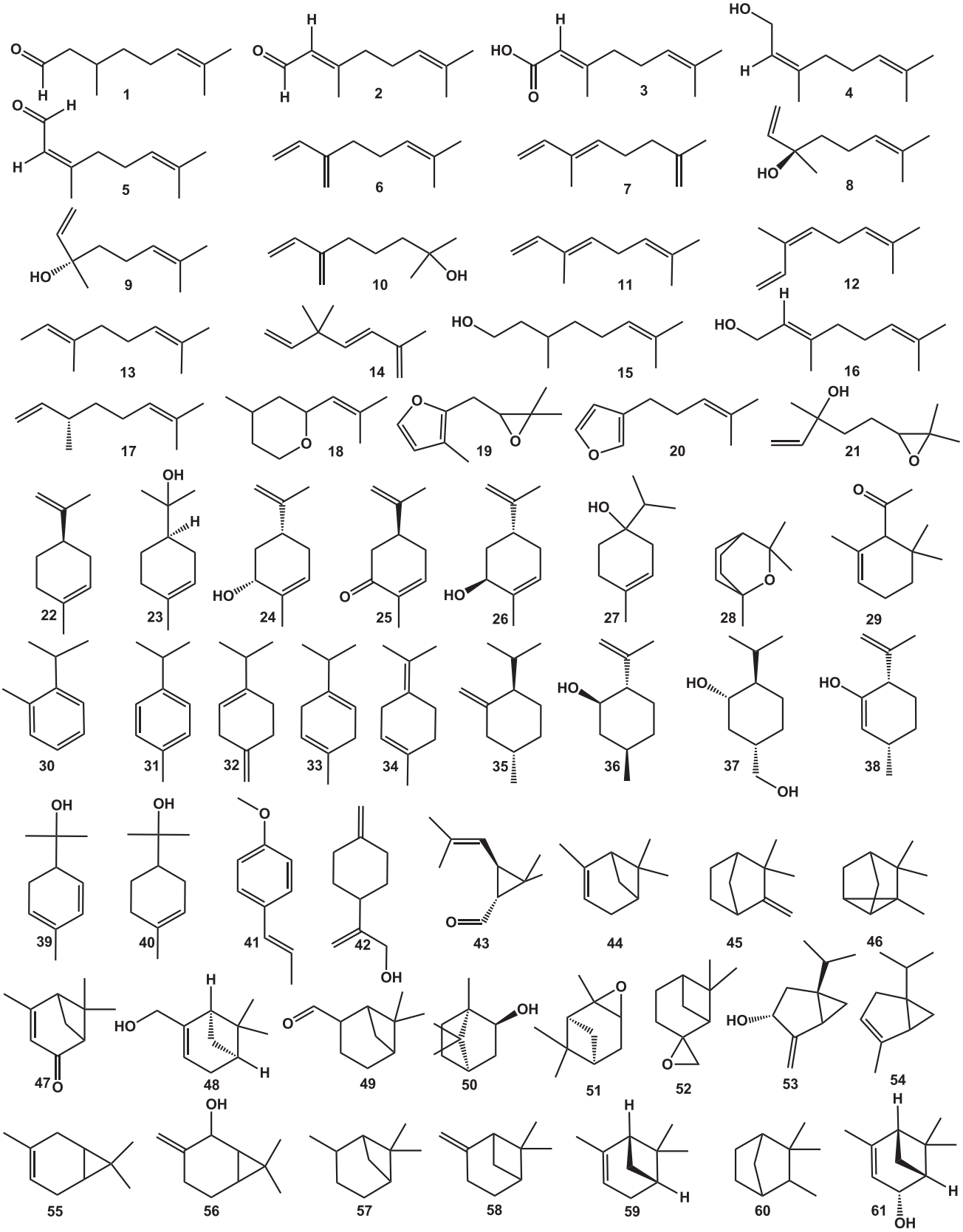

Fig. 1. Chemical structures of monoterpenes from LG.

Table 2
Sesquiterpenes (**62**–**98**) isolated from LG.

No.	Molecular formulas	Compounds	References
62	$C_{15}H_{24}$	α-Farnesene	Ekpenyong, Akpan, & Nyoh, 2015
63	$C_{15}H_{24}$	γ-Muurolene	Ekpenyong, Akpan, & Nyoh, 2015
64	$C_{15}H_{24}$	α-Muurolene/Muurolene	Ekpenyong, Akpan, & Nyoh, 2015
65	$C_{15}H_{24}$	δ-Cadinene	Ekpenyong, Akpan, & Nyoh, 2015
66	$C_{15}H_{24}$	γ-Cadinene	Kouame et al., 2015
67	$C_{15}H_{24}$	Isogermacrene D	Kouame et al., 2015
68	$C_{15}H_{24}$	Germacrene-D	Ekpenyong, Akpan, & Nyoh, 2015
69	$C_{15}H_{26}O$	*epi*-Cubenol	Kouame et al., 2015
70	$C_{15}H_{26}O$	α-Cadinol	Avoseh et al., 2015
71	$C_{15}H_{26}O$	*t*-Cadinol	Ekpenyong, Akpan, & Nyoh, 2015
72	$C_{15}H_{26}O$	*t*-Muurolol	Ekpenyong, Akpan, & Nyoh, 2015
73	$C_{15}H_{26}O$	Isointermedeol	Yang et al., 2020
74	$C_{15}H_{26}O$	β-Eudesmol	Ekpenyong, Akpan, & Nyoh, 2015
75	$C_{15}H_{26}O$	Selina-6-en-4-ol	Avoseh et al., 2015
76	$C_{15}H_{24}$	α-Selinene	Ekpenyong, Akpan, & Nyoh, 2015
77	$C_{15}H_{24}$	Valencene	Ekpenyong, Akpan, & Nyoh, 2015
78	$C_{15}H_{26}O$	Viridiflorol	Ekpenyong, Akpan, & Nyoh, 2015
79	$C_{15}H_{26}O$	Elemol	Ekpenyong, Akpan, & Nyoh, 2015
80	$C_{15}H_{26}O$	α-Elemol	Ekpenyong, Akpan, & Nyoh, 2015
81	$C_{15}H_{24}$	Zingiberene	Kouame et al., 2015
82	$C_{15}H_{24}$	β-Sesquiphellandrene	Ekpenyong, Akpan, & Nyoh, 2015
83	$C_{15}H_{24}O$	β-Caryophyllene oxide	Kouame et al., 2015
84	$C_{15}H_{24}$	β-Caryophyllene	Kouame et al., 2015
85	$C_{15}H_{24}$	α-Gurjunene	Ekpenyong, Akpan, & Nyoh, 2015
86	$C_{15}H_{24}$	Aromandendrene	Kouame et al., 2015
87	$C_{15}H_{24}$	Humulene/α-Humulene	Ekpenyong, Akpan, & Nyoh, 2015
88	$C_{15}H_{24}$	*trans*-α-Bergamotene	Barbosa et al., 2008
89	$C_{15}H_{24}$	α-Santalene	Li et al., 2021
90	$C_{15}H_{26}O$	Juniper camphor	Barbosa et al., 2008
91	$C_{15}H_{24}$	δ-Elemene	Li et al., 2021
92	$C_{15}H_{24}$	α-Cubebene	Li et al., 2021
93	$C_{15}H_{24}$	β-Bourbonene	Kpoviessi et al., 2014
94	$C_{15}H_{24}$	Cuparene	Barbosa et al., 2008
95	$C_{15}H_{24}$	(+)-β-Elemene	Li et al., 2021
96	$C_{15}H_{24}$	(-)-β-Elemene/β-Elemene	Li et al., 2021
97	$C_{15}H_{26}O$	Torreyol	Barbosa et al., 2008
98	$C_{15}H_{26}O$	Eudesm-7(11)-en-4-ol	Kpoviessi et al., 2014

acid (**101**) is an abietane diterpene, an ability-8,11,13-triene substituted by hydroxy groups at positions 11 and 12 and a carboxy group at position 20. The diterpenes and triterpenes isolated from LG are shown in Table 3 and Fig. 3.

3.4. Flavonoids

Only 10 flavonoids, including eight flavonoids (**107**, **110**–**116**) and two flavonols (**108** and **109**), have been identified thus far in research on flavonoids in LG. LG contains six flavonoid glycosides in LG, including three C_6-glycosides, one C_8-glycoside, one O_3-glycoside, and one O_7-glycoside. Detailed information on the flavonoids in LG is shown in Table 4 and Fig. 4.

3.5. Phenolic acids

Phenolic acids are metabolic component containing phenolic hydroxyl and carboxylic acids, with only one benzene ring in the molecule. Based on their carbon skeleton structures, phenolic acids can be divided into hydroxybenzoic acid derivatives (C6–C1 type) and hydroxycinnamic acid derivatives (C6–C3 type). Seven phenolic acids were isolated and identified from LG, of which two (**117** and **118**) were hydroxybenzoic acid derivatives, and five (**119**–**123**) were hydroxycinnamic acid derivatives. Details of the phenolic acids are shown in Table 5 and Fig. 5.

3.6. Polysaccharides

More researchers have focused on polysaccharides in recent years because of their widespread use in healthy foods and medications. The biological effects of LG polysaccharides include immunomodulatory and anti-tumor activities. The polysaccharides in LG include the water-soluble polysaccharides HWSPs (**124**), CCP (**125**), and CCF (**126**), and the acidic polysaccharides F1 (**127**) and F2 (**128**). FTIR analysis further confirmed that HWSP is a polysaccharide containing proteins and uronic acid (Thangam, Suresh, & Kannan, 2014). Unlike HWSPs, neither CCP nor CCF contains proteins, while CCP contains less uronic acid. Analysis of the monosaccharide composition by HPLC showed that CCP was composed of glucose, rhamnose, ribose, galactose, arabinose, xylose, and mannose, with a molar ratio of 6.17:5.90:3.40:2.92:2.31:1.63:1.00 (Bao, Yuan, Wang, Fan, & Lan, 2015; Chen, Qiao, Liu, Xing, & Chen, 2022). F1 and F2 are the polysaccharide fractions containing uronic acid. F1 and F2 comprise xylose, glucose, galactose and mannose, with xylose as the main monosaccharide skeleton (Thangam, Sathuvan, & Kannan, 2014).

3.7. Other compounds

In addition, 30 compounds (**129**–**158**) were isolated from LG, including phenols, phenylpropanoids, esters, alcohols, aldehydes, ketones, alkaloids, and amino acids (Table 6 and Fig. 6).

4. Pharmacology

The effectiveness of LG has been documented in several books. According to *Guangdong Traditional Chinese Medicine*, LG can treat dizziness and phlegm caused by wind, and its water decoction has been used to treat heartache after drinking, owing to its anti-

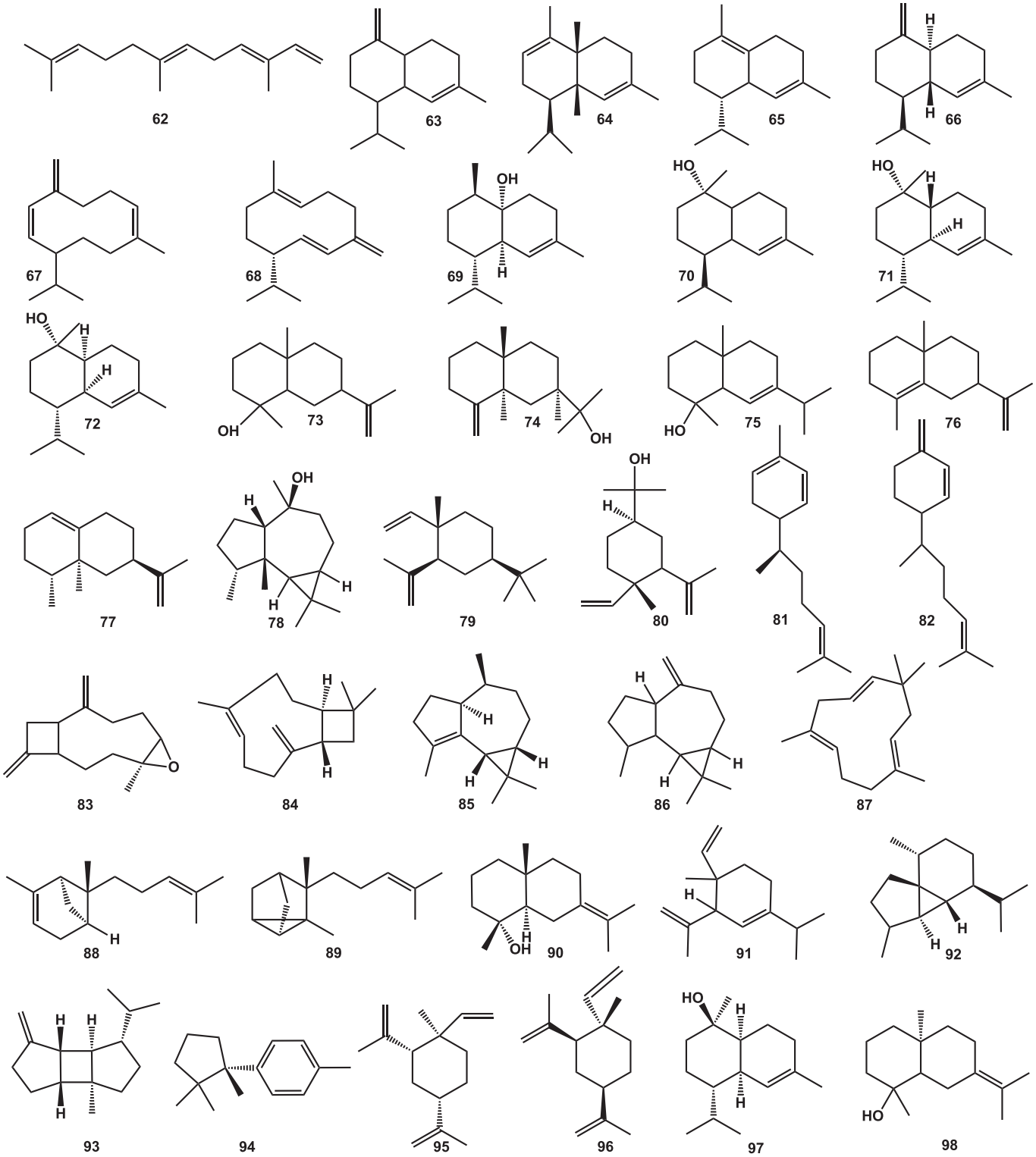

Fig. 2. Chemical structures of sesquiterpenes from LG.

inflammatory and analgesic effects. *The Guizhou Folk Medicine* (*Guizhou Minjian Yaowu* in Chinese) also mentions that LG water decoction can alleviate stomach aches, which affects the digestive tract. Other biological functions of LG have also been found in contemporary pharmacological studies, including antibacterial, neuroprotective, anti-diabetes, antioxidant, free radical scavenging, antitumor, and immunomodulatory effects (Fig. 7).

4.1. Antimicrobial effect

Lemongrass essential oil (LGEO) exhibits good antibacterial activity and expressed inhibitory effects against various bacteria and fungi. These included gram-negative bacteria (*Serratia marcescens*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Chromobacterium violaceum*), gram-positive bacteria (*Staphylococcus aureus*

Table 3
Diterpenes and triterpenes (**99**–**106**) isolated from LG.

No.	Molecular formulas	Compounds	References
99	$C_{20}H_{40}O$	Phytol	Santos Serafim Machado et al., 2015
100	$C_{22}H_{42}O_2$	Phytol acetate	Santos Serafim Machado et al., 2015
101	$C_{20}H_{28}O_4$	Carnosic acid	Barbosa et al., 2008
102	$C_{30}H_{50}O$	Cymbopogonol	Yang et al., 2020
103	$C_{30}H_{50}O$	Cymbopogone	Crawford, Hanson, & Koker, 1975
104	$C_{30}H_{50}O$	Filican-3-one	Crawford, Hanson, & Koker, 1975
105	$C_{30}H_{50}O$	D:A-Friedoursan-3-one	Yang et al., 2020
106	$C_{30}H_{50}O$	Friedelin	Crawford, Hanson, & Koker, 1975

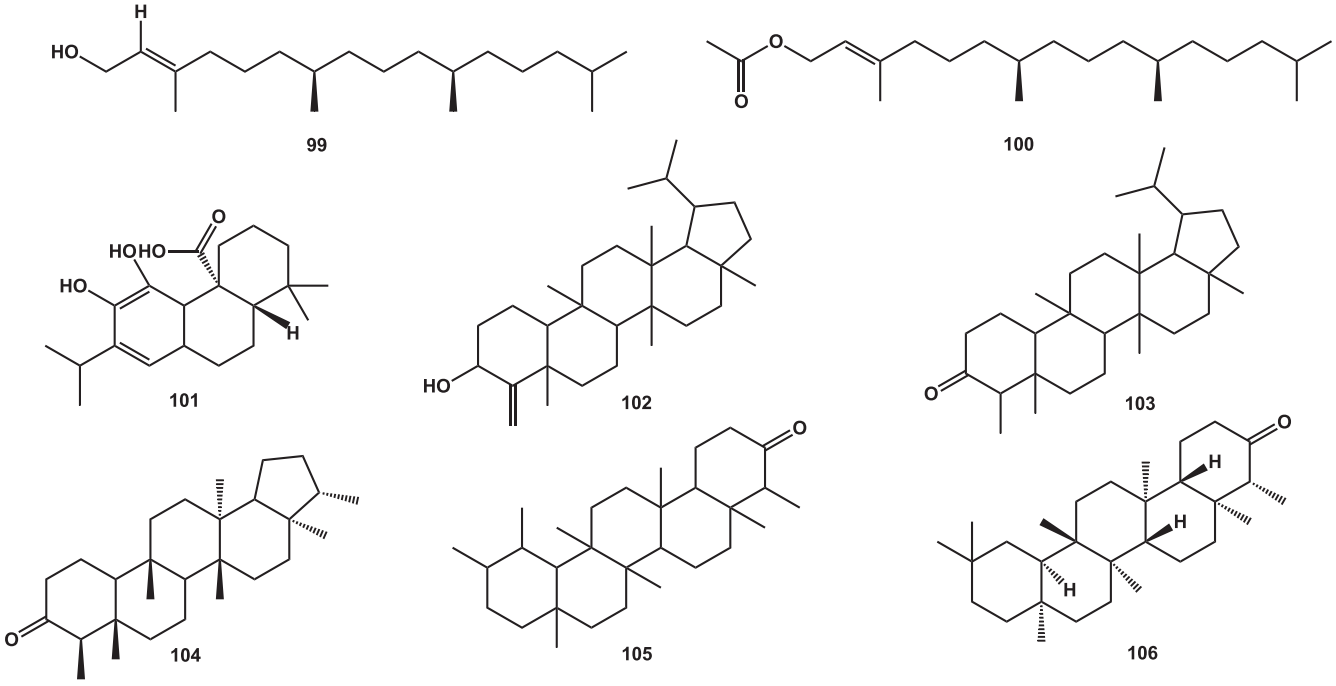

Fig. 3. Chemical structures of diterpenes and triterpenes from LG.

Table 4
Flavonoids (**107**–**116**) isolated from LG.

No.	Molecular formulas	Compounds	References
107	$C_{15}H_{10}O_5$	Apigenin	Ekpenyong, Akpan, & Nyoh, 2015
108	$C_{15}H_{10}O_6$	Kaempferol	Ekpenyong, Akpan, & Nyoh, 2015
109	$C_{15}H_{10}O_7$	Quercetin	Ekpenyong, Akpan, & Nyoh, 2015
110	$C_{15}H_{10}O_6$	Luteolin	Ekpenyong, Akpan, & Nyoh, 2015
111	$C_{22}H_{22}O_{11}$	Isoscoparin	Ekpenyong, Akpan, & Nyoh, 2015
112	$C_{22}H_{22}O_{11}$	Swertiajaponin	Ekpenyong, Akpan, & Nyoh, 2015
113	$C_{21}H_{20}O_{11}$	Luteolin-7-*O*-glucoside	Avoseh et al., 2015
114	$C_{21}H_{20}O_{11}$	Isoorientin	Cheel et al., 2005
115	$C_{21}H_{20}O_{11}$	Orientin	Ekpenyong, Akpan, & Nyoh, 2015
116	$C_{27}H_{30}O_{16}$	Rutin	Meabed, Abou-Sreea, & Roby, 2018

and *Staphylococcus albus*), and fungi (*Candida albicans* and *Candida tropicalis*) (Fig. 8). The antibacterial activity of LGEO is mainly attributed to the presence of active components, including citral, citronellal, citronellol, linalool, and geraniol (Bakkali, Averbeck, Averbeck, & Idaomar, 2008; Ekpenyong, Akpan, & Nyoh, 2015).

Bacteriostasis experiments indicated that when the concentration of LGEO diluted in methanol was 25%, the inhibition rates of LGEO against *S. marcescens* MG1, *S. marcescens* H30, *E. coli*, *S. aureus*, *P. aeruginosa,* and *C. violaceum* were 71.30%, 68.10%, 58.85%, 73.49%, 55.36%, and 100%, respectively. The inhibitory activity of LGEO against gram-negative bacteria was higher than that against gram-positive bacteria, and the inhibition rate increased as the LGEO content increased (Yang et al., 2021). Furthermore, *S. albus* and *C. albicans* were all refrained by LGEO, with minimum inhibitory concentrations (MIC) of 1.188%–2.375% and 2.375%–4.75% and minimum bactericidal concentrations (MBC) of 2.375%–

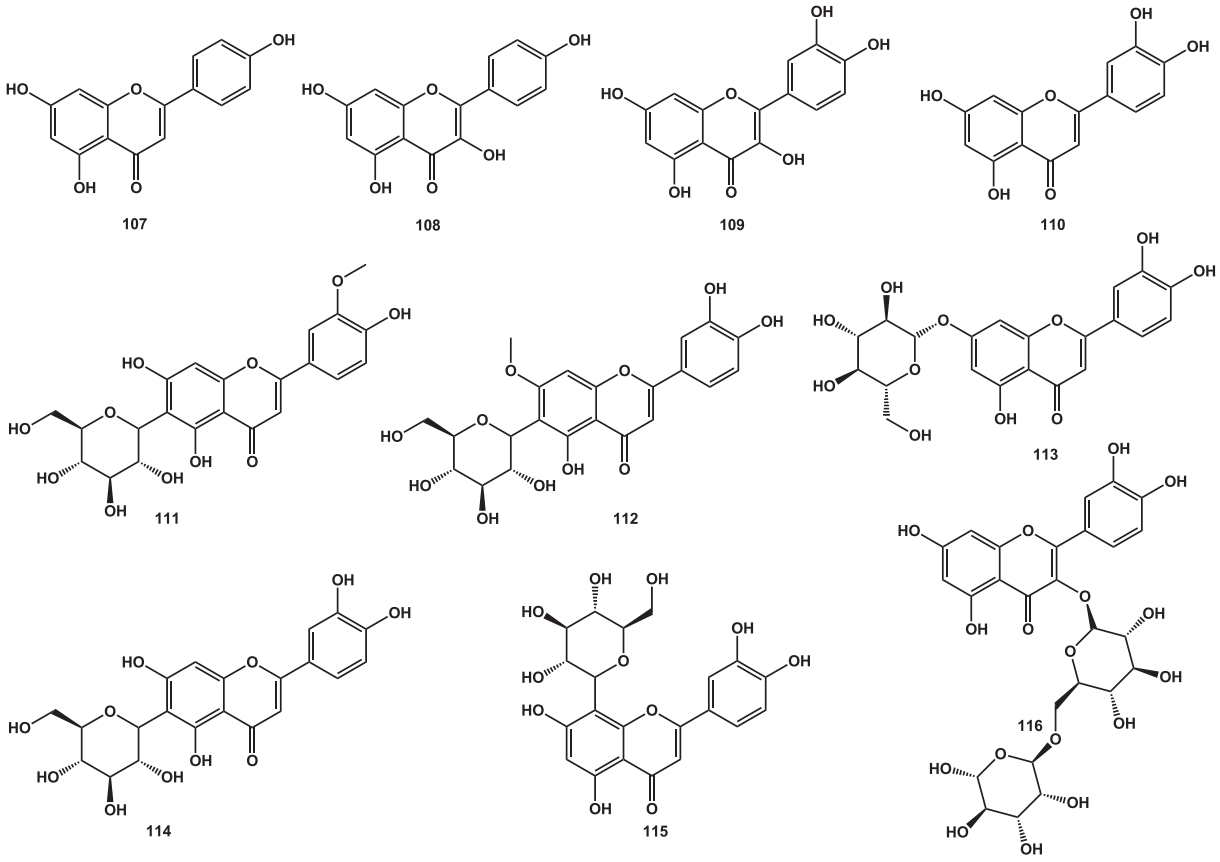

Fig. 4. Chemical structures of flavonoids from LG.

Table 5
Phenolic acids (**117**–**123**) isolated from LG.

No.	Molecular formulas	Compounds	References
117	$C_7H_6O_3$	*p*-Hydroxybenzoic acid	Tapia et al., 2007
118	$C_7H_6O_5$	Gallic acid	Barbosa et al., 2008
119	$C_9H_8O_3$	*p*-Coumaric acid/4-Hydroxycinnamic acid	Ekpenyong, Akpan, & Nyoh, 2015
120	$C_{10}H_{10}O_4$	Ferulic acid	Barbosa et al., 2008
121	$C_9H_8O_4$	Caffeic acid	Ekpenyong, Akpan, & Nyoh, 2015
122	$C_{16}H_{18}O_9$	Chlorogenic acid	Ekpenyong, Akpan, & Nyoh, 2015
123	$C_{16}H_{18}O_9$	Neochlorogenic acid	Tapia et al., 2007

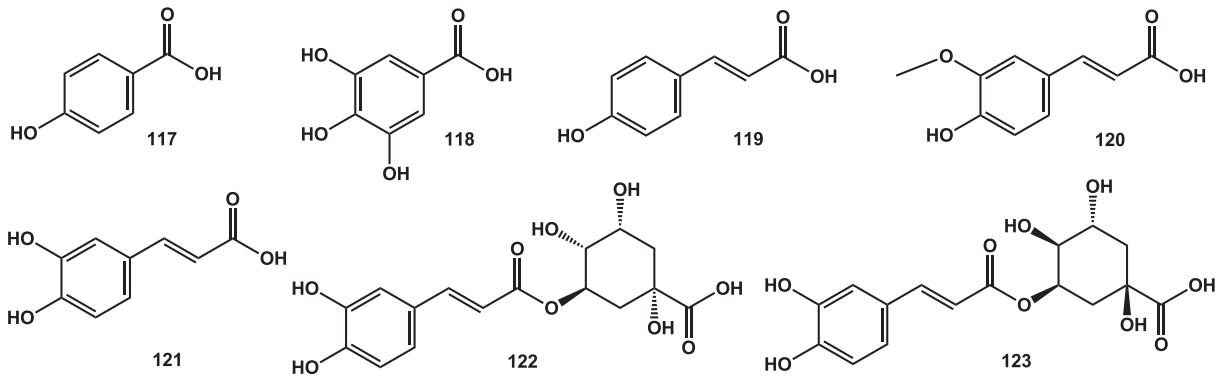

Fig. 5. Chemical structures of phenolic acids from LG.

Table 6
Other compounds (**129**–**158**) isolated from LG.

NO.	Molecular formulas	Compounds	References
129	$C_6H_6O_2$	Catechol	Ekpenyong, Akpan, & Nyoh, 2015
130	$C_6H_6O_2$	Hydroquinone	Avoseh et al., 2015
131	$C_6H_6O_3$	Pyrogallol/Pyrogallic acid	Barbosa et al., 2008
132	$C_8H_8O_3$	Vanillin	Yang et al., 2020
133	$C_{10}H_{12}O_2$	Chavibetol/*M*-Eugenol	Li et al., 2021
134	$C_{10}H_{12}O_2$	Isoeugenol	Kouame et al., 2015
135	$C_{10}H_{12}O_2$	Eugenol	Yang et al., 2020
136	$C_{11}H_{14}O_2$	Methyl eugenol	Yang et al., 2020
137	$C_{12}H_{16}O_3$	Elemicin	Ekpenyong, Akpan, & Nyoh, 2015
138	$C_9H_8O_2$	Cinnamic acid	Barbosa et al., 2008
139	$C_{12}H_{20}O_2$	Neryl acetate	Kouame et al., 2015
140	$C_{11}H_{18}O_2$	Neryl formate	Li et al., 2021
141	$C_{12}H_{20}O_2$	Geranyl acetate	Li et al., 2021
142	$C_{11}H_{18}O_2$	Geranyl formate	Kouame et al., 2015
143	$C_{21}H_{42}O_2$	Eicosanoic acid methyl ester	Santos Serafim Machado et al., 2015
144	$C_{18}H_{27}NO_3$	Capsaicin	Yang et al., 2020
145	$C_8H_{14}O$	6-Methyl-5-hepten-2-one	Ekpenyong, Akpan, & Nyoh, 2015
146	$C_{11}H_{22}O$	Methyl-*n*-nonyl-ketone	Ekpenyong, Akpan, & Nyoh, 2015
147	$C_{13}H_{20}O$	*β*-Ionone	Yang et al., 2020
148	$C_{16}H_{32}O_2$	Palmitic acid	Santos Serafim Machado et al., 2015
149	$C_8H_{16}O$	Octanal	Kpoviessi et al., 2014
150	$C_5H_9NO_4$	Glutamic acid	Tapia et al., 2007
151	$C_5H_6O_2$	Furfurol	Ekpenyong, Akpan, & Nyoh, 2015
152	$C_9H_{18}O$	Nonanal	Lorenzetti, Souza, Sarti, Santos Filho, & Ferreira, 1991
153	$C_{10}H_{20}O$	Decanal	Li et al., 2021
154	$C_8H_{14}O$	1-Octyn-3-ol	Ekpenyong, Akpan, & Nyoh, 2015
155	$C_9H_{16}O$	Melonal	Li et al., 2021
156	$C_{10}H_{18}O$	Nopol	Kpoviessi et al., 2014
157	C_9H_{18}	1-Isopropyl-3-methylcyclopentane	Li et al., 2021
158	$C_{17}H_{28}ClNO$	8-Hmpat	Li et al., 2021

4.75% and 4.75%−9.5% (Niu et al., 2020). Sahal et al. determined the MIC and MBC of LGEO against three types of *C. tropicalis*: *C. tropicalis* T26, *C. tropicalis* U71, and *C. tropicalis* V89. The MIC were 0.2%, 0.1% and 0.39%, and the MBC were 0.39%, 0.1% and 0.39% (Sahal et al., 2020).

A study of the inhibitory effect of LGEO on *C. albicans* activity *in vitro* indicated that the gas-phase antibacterial effect was significantly better than the liquid contact effect. We found that the structure and surface properties of *C. albicans* changed notably after treatment with LGEO. The degree of cell atrophy and surface property changes caused by vapor-phase fumigation are more significant than those caused by liquid contact (Tyagi & Malik, 2010). Ergosterol is the most abundant sterol component in fungal membranes. It is the vital to the structural integrity of the cell membrane and, therefore, is the main target of most available antifungal drugs. The transcriptional regulator gene (ERG), which converts lanolin to ergosterol, is downregulated by citronellol, geraniol, and citronellol, thereby disrupting the fungal cell membrane integrity. Moreover, Citronella disturbs membrane stability by increasing fungal hypersensitivity to membrane disruptors, decreasing ergosterol levels, and reducing glucose-induced H^+ extrusion (OuYang et al., 2021).

4.2. Neuroprotective effect

Numerous studies have demonstrated the neuroprotective properties of LGEO, including its anti-neurotoxicity, anti-convulsant, hypnotic, and anti-anxiety effects. The primary mechanisms by which LGEO exerts its neuroprotective effects include inhibition of oxidative stress and inflammatory responses, alteration of seizure thresholds or prevention of the spread of seizures, reduction of central activity, and regulation of the $GABA_A$ receptor-benzodiazepine complex.

Madi et al. investigated the effects of aqueous LG extracts (125, 250, and 500 mg/kg) and ethanolic extracts (125, 250, and 500 mg/kg) on $AlCl_3$-induced Alzheimer's disease (AD) in rats. Oral administration of LG aqueous extract (250 and 500 mg/kg) and LG ethanolic extract (125 mg/kg) significantly down-regulated $AlCl_3$-induced elevated levels of Aβ (78.38%, 75.51%, and 81.34%), tau protein (86.44%, 79.24%, and 67.80%), malondialdehyde (83.58%, 76.75%, and 80.63%), nuclear factor-kappaB (NF-κB) (74.01%, 63.61%, and 80.82%) and IL-6 (65.82%, 41.69%, and 79.89%) in rats. By decreasing oxidative stress and inflammatory indicators, LG extract reduced $AlCl_3$-induced neurotoxicity in rats. This effect may be partly attributed to the high content of caffeic acid and isoorientin (Madi, Choucry, El-Marasy, Meselhy, & El-Kashoury, 2020).

Adult zebrafish were pretreated, soaked in four samples of *C. citratus* essential oil (EO), aqueous ethanol extract of LG leaves (E1), citral (CIT), and geraniol (GER), and then exposed to a pentylenetetrazole (PTZ) solution to evaluate the anti-convulsant properties of LG. The latent time of the initial convulsion was longer in zebrafish treated with EO (20 mg/L), E1 (3 mg/L), CIT (20 mg/L), GER (20 mg/L), and CIT + GER (5 mg/L) than in the model group. Evaluation of oxidative stress markers in zebrafish brain homogenates showed that the model group had significantly higher levels of malondialdehyde (MDA) and nitric oxide (NO) than the control group. In contrast, glutathione (GSH) and catalase (CAT) levels were remarkably reduced. Compared to the model group, the administration group effectively reduced MDA and NO levels, increased GSH levels, and restored CAT enzyme activity. It has been proven that LG engages in antioxidant pathways that contribute to neuroprotection (Hacke, Miyoshi, Marques, & Pereira, 2021). Another study evaluated the epileptic seizures induced by pentylenetetrazole in mice. Mice treated with LGEO were protected against seizure episodes, reducing the occurrence of seizures to 40% in mice treated with 0.5 g/kg and 20% in mice treated with 1.0 g/kg. LGEO may be effective by changing the course of seizures, meddling with seizure thresholds, or preventing seizures from spreading (Blanco, Costa, Freire, Santos, & Costa, 2009).

LG not only exerts effects on the nervous system through antioxidant and anti-inflammatory mechanisms but is also con-

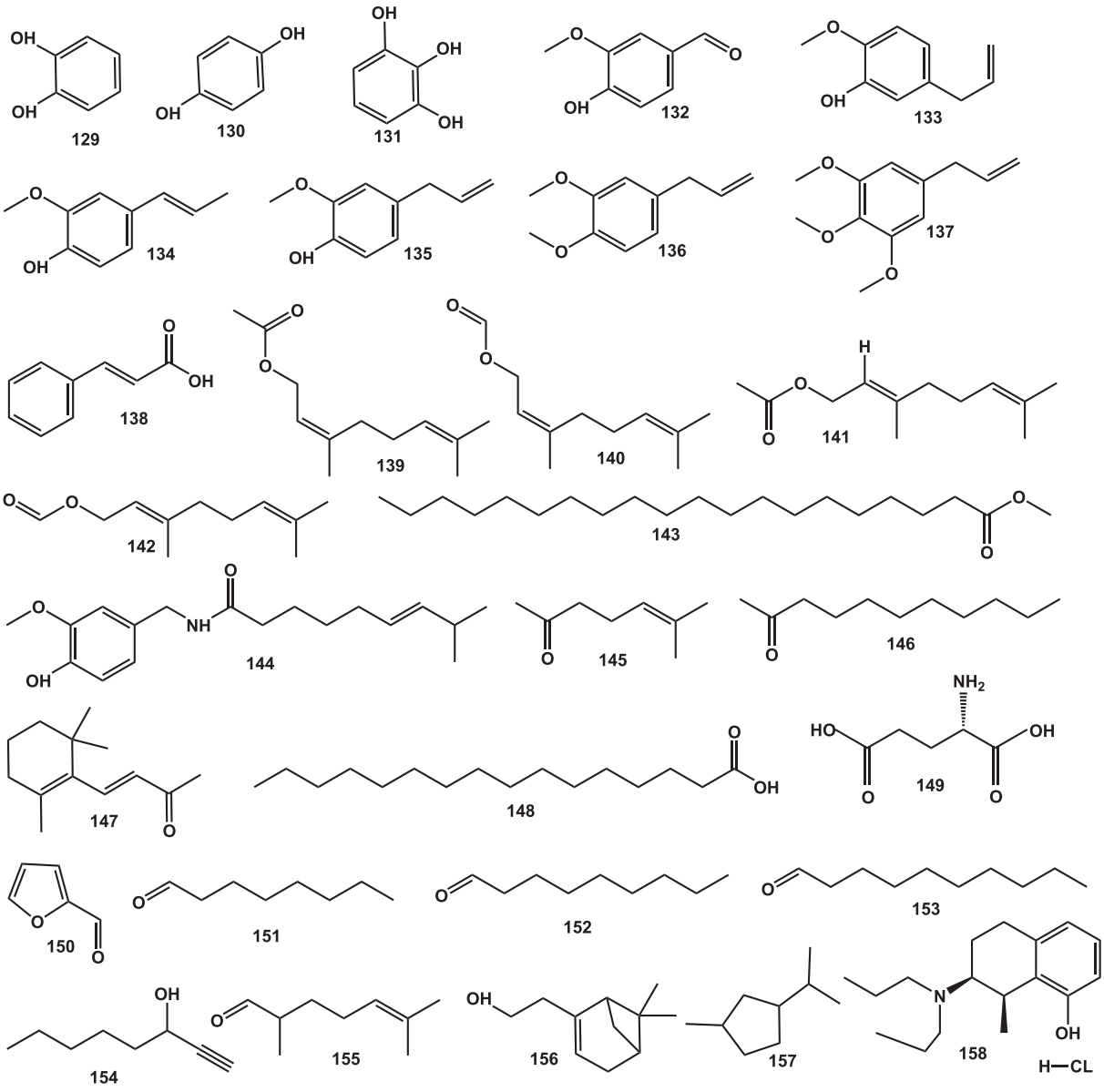

Fig. 6. Other compounds isolated from LG.

sidered an enzyme inducer with central inhibitory activity. After LGEO therapy, pentobarbital sodium elicited decreased sleep latency and increased sleep duration, indicating that LGEO may achieve hypnotic effects by obstructing central nervous system activity. It was discovered that the LGEO group (1.0 g/kg) significantly increased the frequency of open-arm entry and the amount of time spent in a bright room using an elevated labyrinth and a light/dark box program to measure anxiety activity (Blanco, Costa, Freire, Santos, & Costa, 2009). Further studies have shown that the anxiolytic effect of LGEO is related to its regulatory effect on the $GABA_A$-Prozac receptor complex (Yang et al., 2020).

4.3. Antidiabetic effect

According to these studies, LG has an antidiabetic effect, effectively reduces endoplasmic reticulum (ER) stress-induced hyperglycemia, and lowers weight, triglyceride, total cholesterol, and low-density lipoprotein levels in diabetic rats. Rutin is an effective ingredient for reducing blood sugar levels in LG.

ER stress plays a vital role in diabetes pathogenesis. ER stress in rats was induced by streptozotocin (STZ), and rats were treated with LG methanolic leaf extract (100, 200, and 400 mg/kg). Fasting blood glucose (FBG), ER stress-related genes, antioxidants, and pro-inflammatory genes were measured as indicators in diabetic rats. The findings revealed that the methanolic extract of LG significantly decreased FBG levels in diabetic rats and down-regulated GRP78, CHOP, ATF4, TRB3, PERK, IRE1, TNF-α gene manifestation, and up-regulated AhR, Nrf2 gene manifestation. Consequently, STZ-induced ER stress was reduced by LG leaf methanolic extract (100 and 400 mg/kg) through the downregulation of GRP78 and upregulation of NRF2 signaling, thus achieving the effect of reducing blood glucose (Elekofehinti, Onunkun, & Olaleye, 2020).

Ewenighi et al. administered LG extract (1.5 mg/100 g) to diabetic rats for four weeks. There was a prominent increase in high-density lipoprotein levels and a decrease in body weight and blood sugar, triglyceride, total cholesterol, and low-density lipoprotein levels compared to controls (Ewenighi et al., 2013). Meabed et al. determined that the flavonoid content in LG aqueous extract and rutin accounted for 1.843% of the total extract (Meabed, Abou-Sreea, & Roby, 2018). An STZ-nicotinamide rat

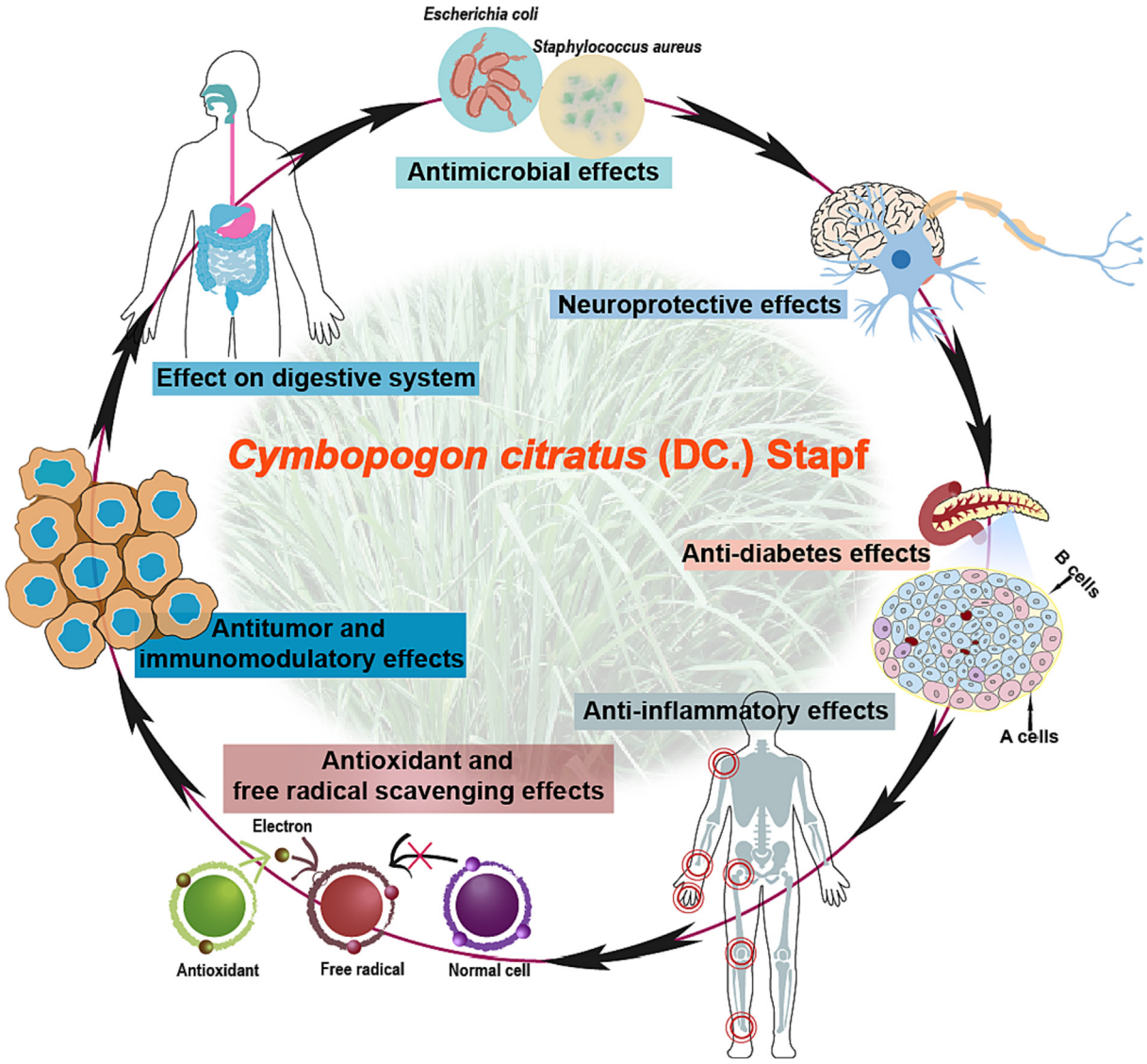

Fig. 7. Modern pharmacological effects of LG.

model of type 2 diabetes showed that rutin possessed hypoglycemic qualities and protected against diabetes complications. The α-glucosidases and α-amylase were blocked by rutin (50 or 100 mg/kg), which can lessen the absorption of carbohydrates in the small intestine. β-Cells were stimulated by rutin (50 mg/kg) to secrete insulin, thus protecting Langerhans islets from deterioration, promoting tissue glucose uptake, and inhibiting gluconeogenesis in the liver (Ghorbani, 2017).

4.4. Anti-inflammation

Francisco et al. evaluated the anti-inflammatory effects of several citronella extract ingredients and discovered that tannins, flavonoids, and phenolic acids have substantial pharmacological effects. Chlorogenic acid (CA), the primary phenolic acid in LG, is a crucial anti-inflammatory substance. It was identified that the expression of cytokines was inhibited by chlorogenic acid through the nuclear factor-κB (NF-κB) pathway, and it was the first time to inhibit the expression of cytokines through the ubiquitin proteasome system. Moreover, CA may exert anti-inflammatory effects by suppressing the activation of p38 mitogen-activated protein kinase (p38 MAPK) and c-Junnh2-terminal kinase (JNK) (Francisco et al., 2013; Francisco et al., 2011; Shen et al., 2021). Recent studies have shown that the natural flavonoid quercetin can reduce the symptoms of multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, and systemic lupus erythematosus in both human and animal models. The levels of neurotoxic and pro-inflammatory mediators in patients with multiple sclerosis were suppressed by quercetin, thereby preventing NF-κB activation. Quercetin also enhances intestinal integrity and hepatic antioxidant capacity, modulates the ERK1/2-FKBP and RXR-STAT3 pathways, increases serum glutathione levels, and inhibits hydrogen peroxide-induced oxidative stress (Francisco et al., 2013; Francisco et al., 2011; Shen et al., 2021). Furthermore, ferulic acid exerts anti-inflammatory effects. The anti-inflammatory effect of ferulic acid (100 mg/kg) was mainly related to the levels of peroxisome proliferator-activated receptor gamma (PPARγ), cell adhesion molecules (CAM), and NF-κB and p38 MAPK signaling pathways. This mechanism is illustrated in Fig. 9 (Li et al., 2021).

Citral is one of the main monoterpenoids in LGEO, which activates peroxisome proliferator-activated receptor (PPAR)- α and γ. Citral inhibits NF-κB activation, and cyclooxygenase-2 (COX-2) communication was inhibited by citral. Campos et al. investigated the role of citral in an experimental mouse model of acute inflam-

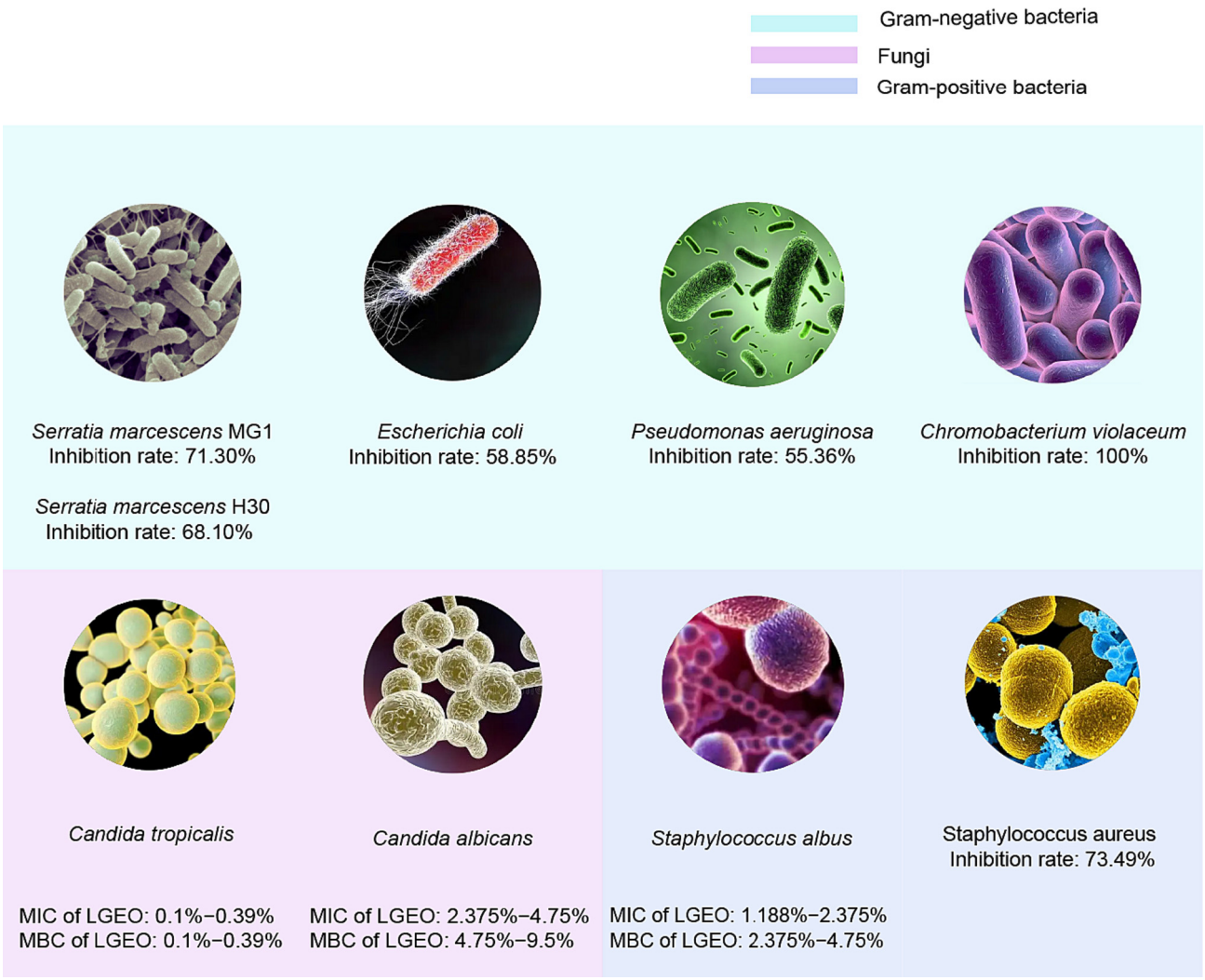

Fig. 8. Antimicrobial effect of LG.

mation and nociceptive hypersensitivity. Citral (50, 100, or 300 mg/kg) markedly inhibited carrageenan-induced paw edema [(57 ± 2.0)%, (70 ± 4.0)%, and (66 ± 3.5)%] and effectively reduced thermal ectopic pain [(62 ± 8.0)%, (80 ± 6.0)%, and (62 ± 3.0)%]. Citral modulates the TLR4 and TLR2/Dectin-1 signaling pathways (Campos et al., 2019; Goncalves et al., 2020). This mechanism is illustrated in Fig. 9.

4.5. Antioxidant and free radical scavenging effects

Studies have shown that antioxidants and free radical scavengers are associated with the prevention of atherosclerosis, heart disease, cancer, arthritis, and other pathologies involving reactive oxygen species (ROS) or free radicals (Middleton, Kandaswami, & Theoharides, 2000). The copper-induced low-density lipoprotein oxidation test showed that LG significantly inhibited Cu^{2+} induced low-density lipoprotein oxidation. The production of active oxidants in human umbilical vein endothelial cells attacked by high *D*-glucose (60% inhibition), hydrogen peroxide (80% inhibition), or oxidized low-density lipoprotein (55% inhibition) decreased LG by 10 and 100 μg/mL (Campos et al., 2014). The polyphenol-rich components of LG, such as chlorogenic acid, caffeic acid, and ferulic acid, have strong antioxidant properties (Khan et al., 2016). The molecular pathway underlying the antioxidant effects of ferulic acid is shown in Fig. 9 (Li et al., 2021).

The 1,1-diphenyl-2-pyridyl propionyl hydrazide (DPPH) assay indicated that the semi-inhibitory concentration (IC_{50}) values for the dichloromethane, ethyl acetate (EtOAc), and methanol extracts of LG were 152, 131, and 41 μg/mL, respectively. The results demonstrated that the LG methanol extract had high antioxidant and free-radical scavenging activity (Cheel et al., 2005).

4.6. Antitumor and immunomodulatory effects

LG was found that had anti-tumor activity and an apparent inhibitory effect on a variety of cancer cells, which was predominantly attributed to its polysaccharide substances (Yang et al., 2020). Mice inoculated with sarcoma 180 (S180) cells were intraperitoneally injected with LG polysaccharide extract (CCPS), and the effects of CCPS on tumor growth, thymus and spleen weights, spleen cell proliferation, and cytokine secretion in tumor-bearing mice were measured seven days later. Mice in the model control group inoculated with S180 gradually experienced negative symptoms, including anorexia, weariness, lethargy, and black hair, due to the rapid growth of tumors. However, these symptoms were markedly diminished in mice treated with CCPS. With dose-dependent inhibition rates of 14.8%, 21.6%, 26.4%, and 37.8% at dosages of 30, 50, 100, and 200 mg/(kg·d), respectively, CCPS considerably slowed tumor growth. At the highest dose of 200 mg/(kg·d), the thymus and spleen weights, splenocyte proliferation, and cytokine secretion in tumor-bearing mice were signifi-

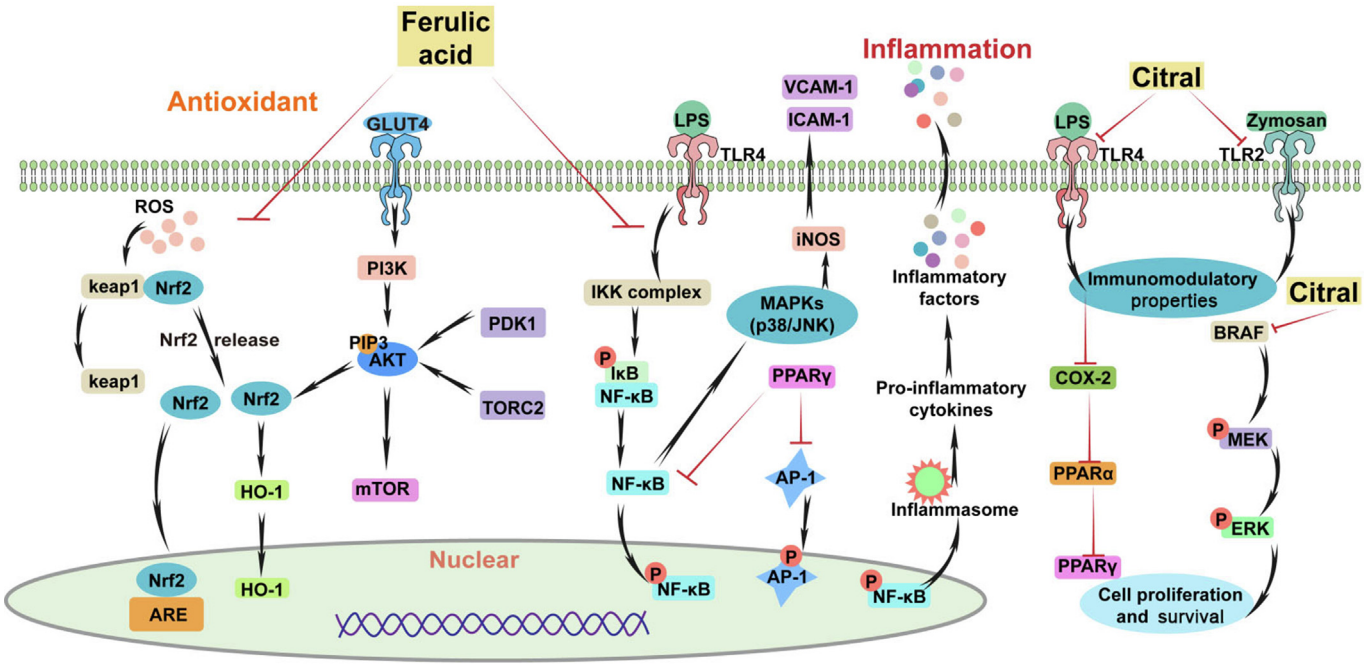

Fig. 9. Anti-inflammation and antioxidant effects of citral and ferulic acid in LG.

cantly increased. However, CCPS was not toxic to S180 cells and was hardly observed. Therefore, CCPS exhibited anti-tumor activity *in vivo*, which may be achieved through immune enhancement rather than direct cytotoxicity (Bao, Yuan, Wang, Fan, & Lan, 2015).

LG had a strong anti-colon cancer effect, in which the ethanol extract induced colon cancer cell apoptosis in a time- and dose-dependent manner without damaging healthy cells *in vitro* and effectively inhibited the growth of xenotransplantation of colon cancer in mice at 16 mg/kg. Additionally, feeding LG ethanol extracts to $APC^{min/+}$ transgenic mice reduced intestinal tumors, indicating its preventive potential (Ruvinov et al., 2019). Gallic acid is an active ingredient of LG used in the fight against colon cancer. In the treatment of colorectal cancer, the combination of gallic acid and anti-PD-1 antibody not only weakened PD-L1/PD-1 signal transduction and reduced Foxp3 stability, but it also encouraged the $CD8^+$ T cell production of IFN-γ and limited tumor development (Deng et al., 2022).

As an anticancer agent, luteolin can fight various human malignant tumors, such as lung, glioblastoma, breast, prostate, and colon cancers. Luteolin can also reverse the epithelial-mesenchymal transition (EMT) through a mechanism involving cytoskeleton shrinkage, induction of the epithelial biomarker E-cadherin indication, and down-regulation of the mesenchymal biomarkers N-cadherin, snail, and vimentin (Imran et al., 2019). Carnosic acid has been extensively studied in oncology both *in vivo* and *in vitro*, and has been shown to have anticancer effects against colorectal, leukemia, kidney, brain, and hepatic cancers (Bahri et al., 2016). Kim et al. indicated a decrease in the viability of human colon cancer HCT116 cells treated with carnosic acid (20 to 100 mmol/L). It triggers HCT116 cell apoptosis via ROS generation, p53 and Bax induction, Caspase3–9 activation, poly (ADP-ribose) polymerase (PARP) cleavage, and STAT3 signaling pathway inhibition (Kim et al., 2016).

4.7. Effect on digestive system

LG has good therapeutic effects on digestive system diseases, including anti-gastric ulcers and liver protection. LGEO and vanillin accelerated the process of gastric healing and demonstrated that the production of gastric mucus was involved in this process. Moreover, geraniol did not inhibit the H^+- and K^+-ATPase activity, although it showed a gastric healing effect at a lower dose (1 μg/mL). In contrast, the H^+- and K^+-ATPase activities were curbed with 100 μg/mL citral, which may be related to their gastric protective effects but cannot ensure the characteristics of gastric healing. Therefore, LGEO and geraniol can potentially gastric ulcers, and citral can effectively prevent gastric injury (Sagradas et al., 2015; Venzon et al., 2018).

Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (γGT) were commonly used indicators for evaluating hepatoprotective effects. Mice with paracetamol (APAP)-induced acute liver injury were orally administered LGEO (125 and 500 mg/kg) for one week. Pretreatment with 125 and 500 mg/kg LGEO significantly reduced the levels of serum markers ALT (95.35% and 97.70%, respectively), AST (91.22% and 94%, respectively), ALP (65.79% and 79.46%, respectively) and γGT (42.63% and 42%, respectively) compared to the APAP group. These results indicated that LGEO exerted protective effects against APAP-induced hepatotoxicity (Uchida et al., 2017).

5. Safety evaluation

The toxicities of LG ethyl acetate, chloroform distillate, essential oils, and pure citral and geraniol components were assessed using *Artemia salina* and human blood cells. Ethyl citrate and chloroform fractions, essential oils, citral, and geraniol were toxic to *A. salina* and human blood cells and could induce changes in the erythrocyte membrane at higher concentrations. Therefore, it is necessary to study these fractions to further determine the phytochemicals related to the observed cytotoxicity and to use an *in vivo* model for exploration. Thus, LG can be used in clinical practice (Hacke et al., 2022).

In a safety assessment experiment, healthy volunteers consumed herbal tea (called Abafador in Brazil) prepared from the dried leaves of LG. After a single dose or oral administration for

two weeks, the Abafador had no change in serum glucose, urea, creatinine, cholesterol, triglycerides, lipids, total bilirubin, indirect bilirubin, glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), alkaline phosphatase, total protein, albumin, lactate dehydrogenase (LDH), and creatine phosphokinase (CPK). Urine analysis, electroencephalographic (EEG), and electrocardiographic (ECG) were normal. Some volunteers showed a slight increase in direct bilirubin and amylase levels; however, no clinical manifestations were observed. These results declared that the LG used in Brazilian folk medicine is non-toxic to the human body (Leite et al., 1986).

6. Applications

6.1. Food applications

LG is frequently used as a flavoring agent in daily life because of its distinctive aromatic flavor and three primary uses (Fig. 10). First, fresh LG stems and leaves were seasoned to eliminate fishy odor, flavor, and oil from chicken, fish, and beef dishes and to improve the freshness and flavor of shellfish and shrimp. LG is also cooked with asparagus, onions, and peas. Second, the LG stems and leaves were processed to produce various flavored products, including LG powder, sauce, salad dressing, hot pot sauce, and cooking oil, which were used to complement the flavor and remove the fishy smell of the foods. Third, when LGEO is extracted as a food additive, it is mainly used for flavoring cakes, honey, milk tea, and other staple and non-staple foods (Qiu et al., 2020).

In foreign countries, LG is used as a seasoning and health tea. Tom Yum is a daily and distinctive food in Southeast Asia. LG, as an indispensable seasoning, has played a role in increasing the brilliant flavor and removing the fishy smell of shrimp and crabs. In Thailand, Malaysia, Vietnam, Brazil, India, and other countries, LG has been developed into a healthy tea to reduce blood pressure. Similarly, many LG-growing provinces in China often convert LG into tea drinks, which have the effects of stomach ventilation and awakening the brain. In addition, LG is often added to fish soup, mutton soup, and hot pot condiments in China because of its pungent flavor. In summer, LG is also added to porridge to prevent heatstroke and improve appetite. The Dai people, an ethnic minority in China, often bind marinated crucian carp and tilapia to LG and slowly bake them with charcoal over a low fire until the fish are ripe. Food tastes fresh, tender and brilliant.

Furthermore, LG can be used as a natural antibacterial agent for food preservation. LGEO has a noticeable inhibition effect on vegetable and fruit decay caused by various molds, such as *Botrytis cinema*, *Penicillium expansum*, *Rhizopus stolonifer*, *Colletotrichum musae*, and *Colletotrichum gloeosporioides* (Arrebola et al., 2010).

6.2. Clinical applications

LG, as a drug and food homologous medicine, is widely used in the food industry and has a long history of clinical application. It can be used externally to treat pediatric fever and pityriasis versicolor and orally or intravenously to treat oral thrush in HIV/AIDS patients.

LG treatment for pediatric fever has remarkable clinical efficacy. A total of 120 patients with exogenous fever were selected from the pediatric outpatient clinic of the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, China. Sixty patients in the control group bathed with warm water, and 60 patients in the treatment group bathed with the Zhuang medicine citronella antipyretic external washing formula. The antipyretic time of the control group was (46.46 ± 2.57) h, and that of the treatment group was (36.17 ± 2.21) h. The antipyretic time in the treatment group was significantly shorter than in the control group (Ye et al., 2018).

LG is made into shampoos or creams for *Pityriasis versicolor*. In the second stage of the study, 47 patients with *P. versicolor* in the treatment group were administered LGEO, and 29 in the control group were administered ketoconazole. After 40 days of treatment, the cure rate of the mold in the treatment group was 60%, whereas that in the control group was > 80%, both of which had therapeutic effects. It is confirmed that LGEO has antifungal effects and can treat *P. versicolor* (Carmo, Pereira, Cavalcante, Gayoso, & Lima, 2013).

In addition to external use, LG is administered orally or intravenously to treat oral thrush in patients with HIV/AIDS. In South Africa, 0.5% aqueous gentian violet solution is the first choice in primary care centers to treat oral thrush in patients with HIV. Ninety HIV-positive patients with oral thrush were randomly divided into three treatment groups: gentian violet, lemon juice and LG. In an analysis of the participants who completed the experiment, the therapeutic effects of lemon juice and LG were better than those of gentian violet (Wright et al., 2009).

LG is clinically used to treat epilepsy, anxiety, diabetes, allergies, rheumatism, arthritis, and other diseases. Their clinical applications are illustrated in Fig. 10.

6.3. Daily chemical applications

In addition to its edible and medicinal value, LG is commonly used in skincare products, hair conditioners, mouthwashes, and insecticides because of its unique aroma and properties.

Different concentrations of LGEO (0.5%, 1.0%, and 1.5%, mass ratio) were added to chitosan film-forming matrices to form bioactive skincare films. The concentrations of LGEO strongly controlled the antioxidant properties and water vapor permeability. Chitosan bioactive films containing 0.5% LGEO showed over 70% cell viability, while bioactive films containing 1.5% LGEO with an antioxidant capacity similar to that of *N*-acetyl-*L*-cysteine showed activity against *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*). LGEO-loaded chitosan biofilms can be used as sheet masks with antioxidant and antibacterial properties for skin care, high elasticity, and selective permeability, and no risk of cytotoxicity (Gaspar et al., 2022).

To evaluate their skincare effects, Unno et al. prepared five LG extracts (80% MeOH, *n*-hexane, ethyl acetate, butanol and water). LG was found to have anti-aging and whitening effects and significant elastase inhibitory activity. The ethyl acetate extract of LG exhibited the highest elastase inhibitory activity. Elastase breaks down elastin (a fibrin), which can damage skin and cause wrinkling. In addition, LG acts as a tyrosinase inhibitor in treating hyperpigmentation. The ethyl acetate extract exhibited the highest lipase inhibitory activity among the LG extracts. Lipase is one of the main virulence factors in acne and hydrolyzes triglycerides to release free fatty acids. Lipase overexpression improves follicular development and causes acne vulgaris (Unno et al., 2017). Therefore, the less lipase secretes, the less acne there is. Many of these compounds have been reported to have antioxidant activity depending on the composition of LG and have been used as cosmetic ingredients (Sarker & Oba, 2020). Protocatechuic acid is a potential skin antiseptic that induces dose-dependent skin penetration and antibacterial activity against acne in mouse skin (Jalali et al., 2020). These results imply that the EtOAc extract of LG is a promising potential skin care cosmeceutical with activity against acne vulgaris (Kim et al., 2022).

LGEO was added to the conditioner to remove dandruff. LGEO was found to be active against lipophilic yeast, and its efficacy and preference were evaluated. LGEO at 5%, 10% or 15% was added to the base formulation with the highest preference. Subjects used the formulation twice daily and efficacy was assessed on days 7 and 14 using the D-Squame® scale. The results revealed that the use of 5%, 10%, or 15% LGEO conditioners significantly reduced dan-

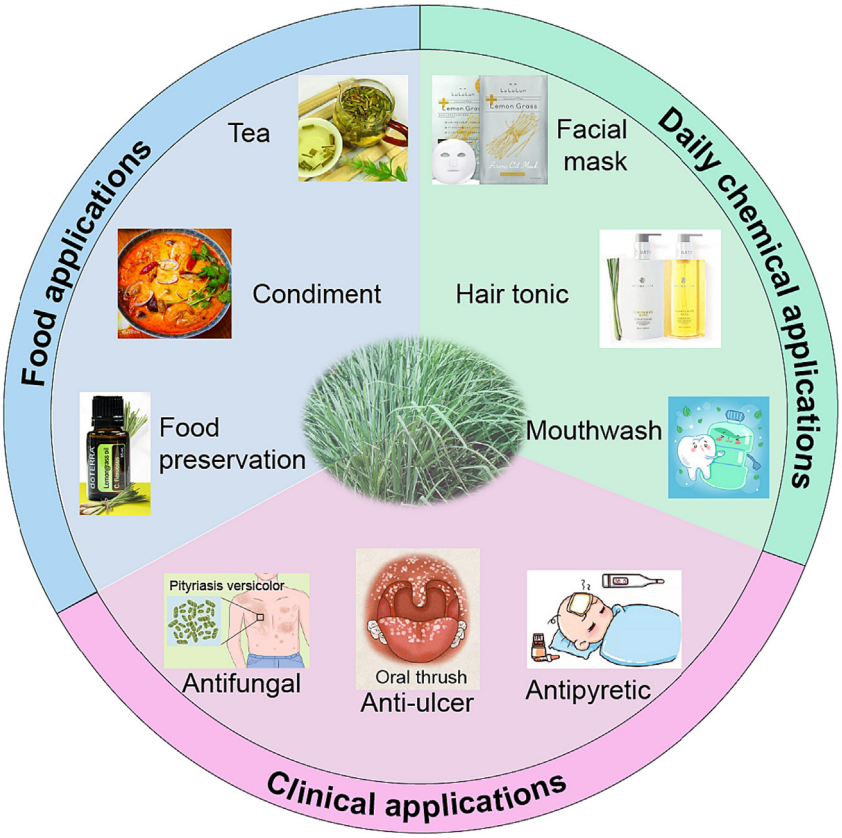

Fig. 10. Applications of LG in food, clinic and daily chemical.

druff ($P < 0.005$) on day 7 (33%, 75%, and 51%, respectively) compared to the blank control, and the effect of reducing dandruff on day 14 (52%, 81%, and 74%, respectively) was more effective ($P < 0.005$). Thus, LGEO is significantly effective in reducing dandruff, with hair care formulations containing 10% LGEO being the most effective (Chaisripipat et al., 2015).

Owing to its antibacterial properties, LG was manufactured as a mouthwash. The antimicrobial activity of the LG mouthwash against common odor-causing microorganisms was tested using broth microdilution and disc diffusion methods. This randomized, double-blind clinical study included 20 healthy volunteers. Volatile sulfur compound levels were measured in each volunteer using a Halimeter on days 0 and 8. The findings showed that, compared to baseline volatile sulphur compounds (VSCs), VSCs levels were remarkably reduced after using the LG mouthwash for 1 min (50.6%) and 7 d (52.1%), while there was no significant reduction with the placebo. This study illustrated that the LG mouthwash significantly reduced oral odor. This mouthwash may be another option to prevent bad breath, plaque formation and gingivitis (Satthanakul et al., 2015).

LGEO has been developed as an insecticide with good repellency, contact, and fumigation effects. It has outstanding advantages for preventing stored grain, food, and health pests. LGEO has good repellent and fumigation effects on *Sitophilus oryzae* L., *Sitophilus zeamais* Motschulsky, *Tribolium indicum*, *Paederus fuscipes* Curtis, *Anopheles rufus*, *Aedes albopictus*, and *Musca domestica* L.. Daily chemical applications of LG are shown in Fig. 10.

7. Summary and prospect

As a drug and food homologous medicine, LG was first recorded in *the Supplement to Materia Medica* with the effects of expelling wind and unblocking collaterals, warming and relieving pain, and draining dampness and diarrhea during the Tang Dynasty (AD 618–907). Phytochemical studies have revealed that LG contains terpenoids, flavonoids, phenolic acids, and other active components. Modern pharmacological studies have shown that LG has many bioactive effects and good development potential, including antibacterial, neuroprotective, hypotensive, hypoglycemic, hypolipidemic, anti-inflammatory, antioxidant, anti-tumor, and other effects for the treatment of pediatric fever, hypertension, stomach disorders, and diabetes. LG is often used as a condiment in food because of its aromatic odor. In the chemical industry, LG is often used to make soaps, detergents, perfumes, skincare products, hair tonics, and mouthwashes. Although the existing research on LG and some of its pharmacodynamic material basis and pharmacological action mechanisms have been elaborated, basic research on action mechanisms and pharmacodynamics is still insufficient and needs further study to facilitate the development and application of LG.

CRediT authorship contribution statement

Xiqin Du: Data curation, Formal analysis, Visualization, Writing – original draft. **Meng Zhang:** Writing – review & editing. **Shuping Wang:** Supervision, Writing – review & editing. **Jingyang Li:** Supervision, Writing – review & editing. **Jingze Zhang:** Conceptualization, Data curation, Project administration, Validation, Writing – original draft, Writing – review & editing. **Dailin Liu:** Conceptualization, Data curation, Project administration, Validation, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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