Biomedical Dermatology

REVIEW Open Access

Advances in research on the active constituents and physiological effects of *Ganoderma lucidum*

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Abstract

Background: *Ganoderma lucidum*, a double-walled basidiospore produced by porous basidiomycete fungi, has been used as a traditional medicine for thousands of years. It is considered a valuable Chinese medicine for strengthening body resistance, invigorating the spleen, and replenishing Qi. *G. lucidum* contains a variety of active ingredients, such as polysaccharides, triterpenoids, nucleosides, sterols, alkaloids, polypeptides, fatty acids, steroids, and inorganic elements, and has anticancer, anti-inflammatory, hepatoprotection, hypoglycemic, anti-melanogenesis, anti-aging, and skin barrier-repairing activity.

Conclusions: The review summarizes the traditional usages, distribution, active constituents, structure, and biological effects of *G. lucidum*, with an aim to offer directions for further research and better usage of *G. lucidum* as a medicinal raw material.

Keywords: *Ganoderma lucidum*, Traditional uses, Polysaccharides, Triterpenoids, Natural products, Pharmacological effect

Background

Ganoderma lucidum is an annual or perennial fungus of the family Ganodermataceae (Campos Ziegenbein et al. 2006); it is commonly known as “Ling Zhi” in China. In the wild, *G. lucidum* mainly grows in subtropical and temperate climate regions such as Asia, Europe, Africa, and Americas (Siwulski et al. 2015). *G. lucidum* has a kidney-shaped cap and its upper surface is russet, with a cloud-like, ring pattern, glossy exterior, and woody texture.

G. lucidum has a systematic theoretical background in traditional Chinese medicine, and research has now confirmed that it contains over 400 bioactive compounds, including polysaccharides, triterpenoids, steroids, fatty acids, amino acids, nucleosides, proteins, and alkaloids (Cör et al. 2018). Polysaccharides and triterpenoids are the major bioactive compounds in *G. lucidum*. The active ingredients and relative pharmacological activities differ during the different growth stages of *G. lucidum*. Modern pharmacology has shown that *G. lucidum* has antitumor (Kao et al. 2016), anti-inflammatory (Liu et al. 2018), and antioxidation effects (Sarnthima et al. 2017) and that it could regulate the respiratory, nervous, and immune systems (Kubota et al. 2018). *G. lucidum* also has a hypoglycemic effect (Tian et al. 2018) and can protect the liver (Wu et al. 2016). Nowadays, *G. lucidum* is used as a powder, tea, and dietary supplement. Therefore, it is extremely significant to study the pharmacological effects and safety of *G. lucidum*.

G. lucidum plays a role in inhibiting tyrosinase activity and tyrosine-related protein expression, and thus, it may ameliorate pigmentation effect (Zhang et al. 2011). It can also anti-aging by inhibiting ultraviolet B (UVB)-induced matrix metalloproteinase (MMP)-1 expression and increasing procollagen expression (Lee et al. 2018). *G. lucidum* also has a marked ability to scavenge free radicals in vivo.

In this review, the traditional pharmacological uses, distribution, main chemical constituents, and pharmacological effects of *G. lucidum* have been summarized. Furthermore, the application of *G. lucidum* in clinic was prospected with an aim to provide references for further development of *G. lucidum*-based resources.

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Distribution and cultivation of *G. lucidum*

Distribution of *G. lucidum*

G. lucidum, a medical fungus, grows in subtropical and temperate climate regions such as Asia, Europe, Africa, and Americas in the wild (Siwulski et al. 2015). In Asia, *G. lucidum* mainly grows in China, Korea, and Japan. In Europe, it is distributed in Sweden, Denmark, and Poland. *G. lucidum* is distributed in Kenya, Tanzania, and Ghana in Africa (Wang et al. 2012). In China, *G. lucidum* grows in the regions around Yangtze and Yellow rivers (Chen and Li 2004). It originated from the Dabie Mountains, which recorded in *Compendium of Materia Medica*.

Cultivation of *G. lucidum*

Owing to the varying quality of *G. lucidum* in the wild and the increasing demand for it in the food service, pharmaceutical, cosmetics, and health product industries, cultivation has become a major source of the mushroom. Different active substances have been extracted from the fruiting bodies, mycelia, and spores of *G. lucidum*. The fruiting bodies of *G. lucidum* have been commonly cultivated on hardwood logs, stumps, and sawdust (Cilerdzic et al. 2018). Artificial cultivation of *G. lucidum* takes a long time, and its quality is susceptible to environmental conditions. Liquid- and solid-state fermentation are popular for the production of mycelia (Zhou et al. 2012), and the secondary metabolites of *G. lucidum* can be obtained quickly by fermentation technology.

Traditional uses of *G. lucidum* in China

According to the colors of the fruiting bodies, *G. lucidum* can be classified into red, black, blue, white, yellow, and purple Reishi, and red Reishi (*G. lucidum*) has shown the most significant health-enhancing effects (Cör et al. 2018). *G. lucidum* has been extensively used as a traditional medicine to promote health and longevity in China. In traditional Chinese medicine, *G. lucidum* is regarded as a valuable for strengthening body resistance, invigorating the spleen, and replenishing Qi. *G. lucidum* was first recognized more than 2400 years ago in *Shen Nong's Materia Medica*, and the book records that *G. lucidum* can improve eyesight, nourish liver qi, improve vital essence, and strengthen bones and muscles. Further, in *Compendium of Materia Medica*, *G. lucidum* has been recorded as being able to preserve the spirit and longevity. Modern studies have shown that *G. lucidum* polysaccharides (GLPs) and *Ganoderma* triterpenoids (GTs) which improve immunity and exert anti-aging effects are the main contributors to the traditional pharmacological activities of *G. lucidum*. *G. lucidum* has been included in the *Chinese Pharmacopoeia* and in the *American Herbal Pharmacopoeia and Therapeutic Compendium* (Hapuarachchi et al. 2018).

Active compounds of *G. lucidum*

Modern studies have shown that *G. lucidum* contains many active compounds, including triterpenoids, polysaccharides, steroids, fatty acids, amino acids, nucleosides, proteins, and alkaloids. The triterpenoids and polysaccharides have attracted considerable attention because of their high content in the fungus, diverse structures, and significant bioactivities.

Polysaccharides

Polysaccharides are extracted from the mycelium, fruit body, and fermentation liquid of *G. lucidum.* The different growth stages of *G. lucidum* are marked by different components, structures, molecular weights, and effects of GLPs. The content of polysaccharides in the mycelium is the highest while that in the fruiting body is the lowest. The monosaccharides in the fruiting bodies are mainly glucose and galactose, while that from the mycelium and spores is mainly glucose (Khanna et al. 2012). GLPs extracted from fruiting bodies can exert anticancer effects via immunomodulation. Various types of polysaccharides, with molecular weights ranging from 4×10^5 to 1×10^6 Daltons (Bishop et al. 2015), have been identified in the fruiting body and mycelia of *G. lucidum* (Khanna et al. 2012; Ferreira et al. 2015). The basic framework of GLPs comprises a high-molecular-weight β-(1→3)-d-glucan with (1→6)-β-d-glucosyl branches (Liu et al. 2014), and the main components of sugars are mannose, rhamnose, glucose, and galactose. The possible repeating units of *G. lucidum* glucans is shown in Fig. 1 (Sone et al. 1985).

Triterpenoids

More than 200 triterpenes have been identified from the fruiting bodies, spores, and mycelia of *G. lucidum* (Baby et al. 2015; Xia et al. 2014). The fruiting body of *G. lucidum* has a high content and wide variety of GTs, while the mycelium has few GTs species. GTs have not be detected in non-broken spores of *G. lucidum* (Yu et al. 2016). All triterpenes are tetracyclic triterpenes (Xia et al. 2014). According to the functional groups and side chains, GTs can be divided into compounds including ganoderic acid, ganoderiol, ganoderone, ganolactone, and ganoderal (Baby et al. 2015). The skeletal types of Ganoderma triterpenoids in *G. lucidum* are shown in Fig. 2. The names and corresponding sources of the compounds are shown in Tables 1, 2, 3, 4, 5, 6, and 7 (Baby et al. 2015; Xia et al. 2014).

Steroids

Thus far, more than 20 types of sterols have been found in *G. lucidum*, and their skeletons can be divided into ergosterols and cholesterols (Baby et al. 2015). The steroid components of *G. lucidum* are summarized in Table 8 (Baby et al. 2015).

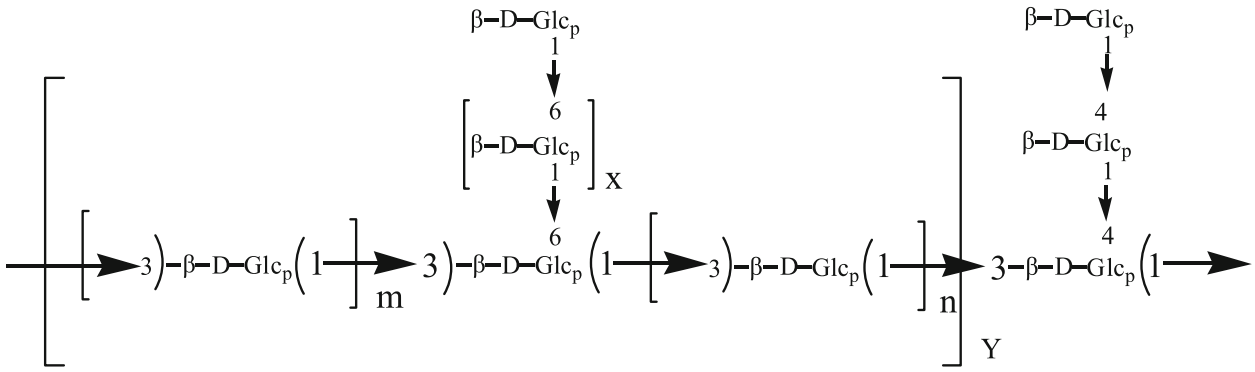


Fig. 1 Possible repeating units of *G. lucidum* glucans. (figure adapted from [21])

Others

Proteins and polypeptide

Several bioactive proteins from *G. lucidum* have been reported. Ling Zhi-8 (LZ-8) is a polypeptide consisting of 110 amino acid residues with an acetylated amino terminus (Lin et al. 2011). The sequence and predicted secondary structure of LZ-8 is very similar to the variable region of the heavy chain of immunoglobulins. LZ-8 was the first immunomodulatory protein obtained from the mycelial extract of *G. lucidum* by using chromato-graphic and electrophoretic techniques (Ahmad 2018).

Enzymes

β-N-Acetylhexosaminidase, α-1,2-mannosidase, endo-β-1,3-glucanase, β-1,3-glucanase, and glutamic protease were extracted from *G. lucidum*, and glutamic protease is the major protein in the extracts of *G. lucidum* (Kumakura et al. 2019).

Nucleosides

G. lucidum also contains nucleosides such as adenosine, cystidine, guanosine, inosine, thymidine, and uridine as well as nucleotides, including adenine, guanine, hypoxanthine, thymine, and uracil (Gao et al. 2007).

Amino acids

Eighteen kinds of amino acids have been found in *G. lucidum*, and the most abundant amino acid was leucine, which possessed strong hypoglycemic and antioxidant activities (Zhang et al. 2018a, 2018b).

Vitamins and minerals

Several vitamins have been reported from *G. lucidum*, such as vitamins B1, B2, B6, β-carotene, C, D, and E. Moreover, various minerals such as calcium, sodium, potassium, phosphorus, iron, carbon, magnesium, zinc, chromium, arsenic, copper, manganese, silicon, aluminum, cobalt, molybdenum, nickel, and lead have been identified in *G. lucidum* (Ahmad 2018).

Physiological activity of *G. lucidum*

Modern medical research has shown that *G. lucidum* contains a variety of compounds with anticancer (Kao et al. 2016), hypoglycemic (Yang et al. 2018), liver protection (Zhao et al. 2019), and anti-inflammatory (Hasnat et al. 2015) effects. Studies also suggest that *G. lucidum* possesses strong antioxidant (Lee et al. 2016) anti-melanogenesis (Hsu et al. 2016), anti-aging (Zeng et al. 2017), and skin barrier-repairing (Montalbano 2018) properties. Thus, *G. lucidum* is important as the lead for the development of pharmaceuticals, nutraceuticals.

Anticancer effects

It has been reported that GLPs, GTs, and extracts of *G. lucidum* have inhibitory effects on cancers, such as prostate cancer (Kao et al. 2016), lung cancer (Chen et al. 2016), glioma (Wang et al. 2018), breast cancer (Smina et al. 2017), and malignant melanoma (Zheng et al. 2018). The underlying mechanisms for the inhibition of these tumors have also been elucidated.

Whiskey and rice wine extracts of *G. lucidum* with growth inhibitory effects against prostate cancer cell lines were identified. The extracts exerted their effects by inhibiting the cell cycle, inducing apoptosis, and reducing tumor progression (Kao et al. 2016). An ethanol extract of sporoderm-broken spores of *G. lucidum* arrested the cell cycle at the G2/M phase and triggered apoptosis by decreasing the expression and activity of cell cycle regulators. It inhibited the survival and migration of human lung cancer cells in a dose-dependent manner, through inhibition of the protein kinase B (Akt) and mammalian target of rapamycin (mTOR) signaling pathway (Chen et al. 2016).

The antitumor effects of GLPs were evaluated on the immune system of rat models of glioblastoma. GLPs increased the concentration of serum interleukin-2 (IL-2), tumor necrosis factor-α (TNF-α), and interferon-γ (INF-γ); the cytotoxic activity of natural killer and T cells; and the functional maturation of dendritic cells, thus

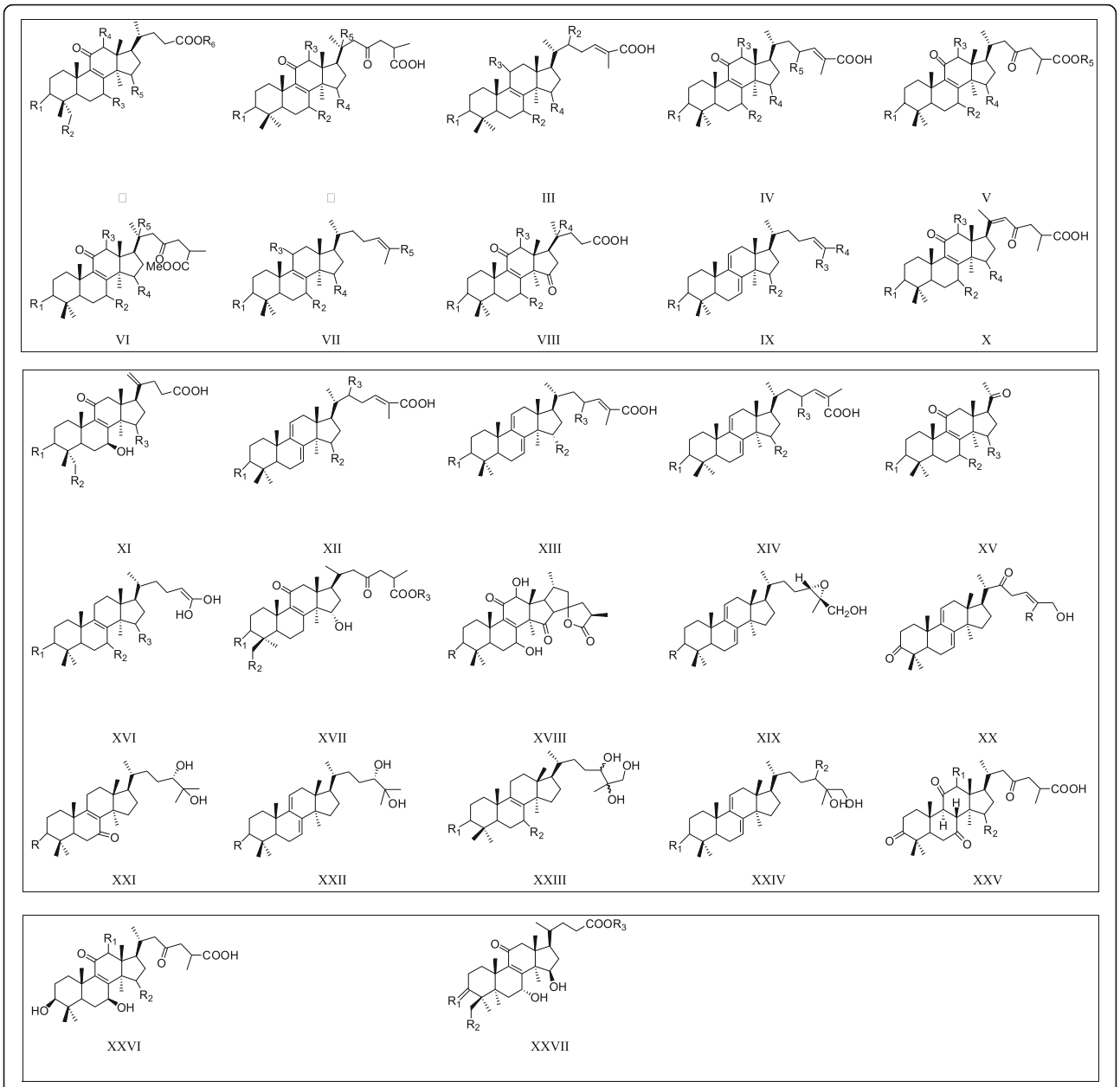


Fig. 2 Skeletal types of Ganoderma triterpenoids in *G. lucidum*

resulting in the inhibition of glioma growth (Wang et al. 2018). Total triterpenes induced apoptosis in human breast adenocarcinoma cells by downregulating the levels of cyclin D1, B cell lymphoma-2 (Bcl-2), AND B cell lymphoma-extra large (Bcl-xL) and upregulating the levels of Bax and caspase-9 (Smina et al. 2017). 9,11-Dehydroergosterol peroxide from *G. lucidum* mycelium inhibited human malignant melanoma cells by participating in the process of decreasing the expression of the myeloid leukemia cell differentiation protein Mcl-1, damaging the mitochondrial membrane, and releasing cytochrome-c (Zheng et al. 2018).

The above studies confirmed that the alcohol extract, total triterpenes, and GLPs have antitumor activity. GTs inhibited cytotoxicity by inhibiting the proliferation and metastasis of cancer cells. *G. lucidum* used as supplements in cancer chemoprevention and chemotherapeutic regimens could be beneficial for the treatment and prevention of various cancers as an adjunct therapy.

Hepatoprotection

The active ingredients in *G. lucidum*, such as GLPs and GTs, can act on the immune system and effectively exhibit hepatoprotective effects and treat liver damage.

Table 1 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	R_1	R_2	R_3	R_4	R_5	R_6	Source
1	Lucidenic acid H	I	β-OH	OH	β-OH	H	O	H	Fruit body
2	Lucidenic acid L	I	β-OH	H	O	β-OH	O	H	Fruit body
3	Lucidenic acid I	I	β-OH	OH	O	H	O	H	Fruit body
4	Lucidenic acid J	I	β-OH	OH	O	β-OH	O	H	Fruit body
5	Lucidenic acid K	I	O	H	O	α-OH	O	H	Fruit body
6	Lucidenic acid M	I	β-OH	H	α-OH	H	α-OH	H	Fruit body
7	Methyl lucidenate I	I	β-OH	OH	O	H	O	Me	Fruit body
8	Methyl lucidenate J	I	β-OH	OH	O	β-OH	O	Me	Fruit body
9	Methyl lucidenate K	I	O	H	O	α-OH	O	Me	Fruit body
10	Methyl lucidenate L	I	β-OH	H	O	β-OH	O	Me	Fruit body
11	Methyl lucidenate M	I	β-OH	H	α-OH	H	α-OH	Me	Fruit body
12	Methyl lucidenate A	I	O	H	β-OH	H	O	Me	Mycelia
13	Methyl lucidenate C	I	β-OH	H	β-OH	β-OH	O	Me	Fruit body
14	Methyl lucidenate F	I	O	H	O	H	O	Me	Mycelia
15	Methyl lucidenate N	I	β-OH	H	β-OH	H	O	Me	Fruit body
16	Methyl lucidenate P	I	β-OH	H	β-OH	β-OAc	O	Me	Fruit body
17	Methyl lucidenate Q	I	O	H	β-OH	H	α-OH	Me	Fruit body
18	Bethyl lucidenate H	I	β-OH	OH	β-OH	H	O	Me	Fruit body
19	Methyl lucidenate D_2	I	O	H	O	β-OAc	O	Me	Fruit body
20	Ethyl lucidenate A	I	O	H	β-OH	H	O	Et	Fruit body
21	Butyl lucidenate A	I	O	H	β-OH	H	O	Bu	Fruit body
22	Butyl lucidenate N	I	β-OH	H	β-OH	H	O	Bu	Fruit body
23	t-Butyl lucidenate B	I	O	H	β-OH	β-OH	O	Bu	Fruit body
24	Butyl lucidenate P	I	β-OH	H	β-OH	β-OAc	O	Bu	Fruit body
25	Butyl lucidenate Q	I	O	H	β-OH	H	α-OH	Bu	Fruit body
26	Butyl lucidenate D_2	I	O	H	O	β-OAc	O	Bu	Fruit body
27	Butyl lucidenate E_2	I	β-OH	H	O	β-OAc	O	Bu	Fruit body
28	*n*-Butyl lucidenate A	I	O	H	β-OH	H	O	Me	Fruit body
29	*n*-Butyl lucidenate N	I	β-OH	H	β-OH	H	O	H	Fruit body
30	Methyl lucidenate E_2	I	β-OH	H	O	OAc	O	Me	Fruit body
31	7,15-Dihydroxy-4,4,14-trimethyl-3,11-dioxochol-8-en–24-oic acid	I	O	H	OH	H	OH	H	Fruit body

The hepatoprotective effects of *G. lucidum* have been widely studied. GLPs can protect hepatocyte injury induced by CCl4 by inhibiting lipid peroxidation, elevating antioxidant enzyme activity, and suppressing apoptosis and immune inflammatory response (Liu et al. 2015). GTs can significantly increase the relative cell viability by 13.46% and reduce the levels of alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase by 51.24%, 33.64%, and 24.07%, respectively, in a culture medium. GTs offered significant cytoprotection against the oxidative damage induced by tertbutyl hydrogen peroxide (t-BHP) in hepatocellular carcinoma cells by decreasing the level of malondialdehyde and increasing the contents of glutathione and superoxide dismutase (SOD) (Wu et al. 2016). *Ganoderma* submerged fermentation reduced ethanol-induced steatohepatitis by decreasing the expression of inflammatory mediators (Chung et al. 2017). Analysis of histopathology and serum enzymes in mice revealed an important hepatoprotective function for the ethanol extract of *G. lucidum* (GLE). GLE inhibited lipid peroxidation, elevated the activity of antioxidant enzymes, and suppressed apoptotic cell death and immune inflammatory responses. It was therefore assumed that GLE can improve alcohol-induced liver injury (Zhao et al. 2019). Previous studies have concluded that *G. lucidum* protects hepatocytes from damage by inhibiting lipid

Table 2 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	R_1	R_2	R_3	R_4	R_5	Source
32	Ganoderic acid A	II	O	β-OH	H	α-OH	H	Fruit body
33	Ganoderic acid B	II	β-OH	β-OH	H	O	H	Fruit body/ Spore
34	Ganoderic acid C_1	II	O	β- OH	H	O	H	Fruit body/ spore
35	Ganoderic acid C_2	II	β-OH	β-OH	H	α-OH	H	Fruit body/ spore
36	Ganoderic acid C_6	II	β-OH	O	β-OH	O	H	Fruit body
37	Ganoderic acid D1	II	O	β- OH	β-OH	O	H	Fruit body
38	Ganoderic acid E	II	O	O	H	O	H	Fruit body/ spore
39	Ganoderic acid F	II	O	O	β-OAc	O	H	Fruit body
40	Ganoderic acid G	II	β-OH	β- OH	β-OH	O	H	Fruit body
41	Ganoderic acid H	II	β-OH	O	β-OAc	O	H	Fruit body
42	Ganoderic acid I	II	β-OH	β-OH	H	O	ξ-OH	Fruit body
43	Ganoderic acid J	II	O	O	H	α-OH	H	Fruit body
44	Ganoderic acid K	II	β-OH,	β-OH	β-OAc	O	H	Fruit body
45	Ganoderic acid M	II	O	β-OH	α-OH	O	H	Fruit body
46	Ganoderic acid N	II	O	β-OH	H	O	ξ-OH	Fruit body
47	Ganoderic acid L	II	β-OH	β-OH	H	α-OH	ξ-OH	Fruit body
48	Ganoderic acid AM_1	II	β-OH	O	H	O	H	Fruit body
49	Ganoderic acid O	II	O	O	H	O	ξ-OH	Mycelium
50	Ganoderic acid B8	II	O	α-OH	H	α-OH	H	Fruit body
51	Ganoderic acid C6	II	β-OH	O	β-OH	O	H	Mycelia
52	Ganoderic acid α	II	β-OH,	O	β-OAc	β-OH	H	Fruit body
53	12-Hydroxylganoderic acid C2	II	β-OH,	β-OH	OH	α-OH	H	Fruit body
54	20-Hydroxylganoderic acid G	II	β-OH	β-OH	β-OH	O	OH	Fruit body
55	3-O-Acetylganoderic acid B	II	β-OAc	β-OH	H	O	H	Mycelia
56	3-Acetylganoderic acid H	II	β-OAc	O	β-OAc	O	H	Fruit body
57	3-O-Acetylganoderic acid K	II	β-OAc	O	H	α-OH	H	Mycelia
58	12-Acetoxyganoderic acid D	II	O	β-OH	OAc	O	H	Fruit body
59	12-Hydroxyganoderic acid D	II	O	β-OH	OH	O	H	Fruit body
60	12-Acetoxyganoderic acid F	II	O	O	β-OAc	O	H	Fruit body
61	Compound B9	II	β-OH	α-OH	H	α-OH	H	Gill
62	Ganolucidic acid A	II	O	H	H	α-OH	H	Fruit body
63	Ganolucidic acid B	II	β-OH	H	H	α-OH	H	Fruit body
64	12β-Hydroxy-3,7,11,15,23-Pentaoxo-5α-lanosta-8-en-26-oic acid	II	O	O	β-OH	O	H	Fruit body
65	12-Hydroxy-3,7,11,15,23-pentaoxo-lanost-8-en-26-oic acid	II	O	O	OH	O	H	Fruit body
66	12,15-Bis(acetyloxy)-3-hydroxy-7,11,23-trioxo-lanost-8-en-26-oic acid	II	OH	O	OAc	OAc	H	Fruit body

Table 2 *Ganoderma* triterpenoids in *G. lucidum (Continued)*

No.	Compound name	Types	R_1	R_2	R_3	R_4	R_5	Source
70	Ganoderic acid W	III	α-OAc	α-OH	H	α-OAc	H	Fruit body
71	Ganoderic acid U	III	α-OH	α-OH	H	H	H	Mycelia
72	Ganoderic acid V	III	O	α-OH	H	α-OAc	H	Mycelia
73	Ganoderic acid Z	III	β-OH	H	H	H	H	Mycelia
74	Ganoderic acid Ma	III	α-OAc	α-OAc	H	α-OH	H	Fruit body
75	Ganoderic acid Mb	II	α-OAc	α-OH	H	α-OAc	ξ-OAc	Fruit body
76	Ganoderic acid Mc	III	α-OAc	α-OAc	H	α-OH	ξ-OAc	Mycelia
77	Ganoderic acid Md	III	α-OAc	α-OMe	H	H	ξ-OAc	Fruit body
78	Ganoderic acid Mg	III	α-OAc	α-OMe	H	α-OH	ξ-OAc	Mycelia
79	Ganoderic acid Mh	III	α-OAc	α-OH	H	α-OH	ξ-OAc	Mycelial
80	Ganoderic acid Mi	III	α-OAc	α-OMe	H	α-OH	H	Mycelia
81	Ganoderic acid β	III	β-OH	β-OH	O	O	H	Spore
82	7-O-Methyl ganoderic acid O	III	α-OAc	α-OMe	H	α-OAc	β-OAc	Mycelia
83	7-O-Ethyl ganoderic acid O	III	α-OAc	α-OEt	H	α-OAc	ξ-OAc	Mycelia
84	7-Oxo-ganoderic acid Z	III	β-OH	O	H	H	H	Fruit body
85	3α,22β-Diacetoxy-7α-hydroxyl-5α-lanost-8,24E-dien-26-oic acid	III	α-OAc	α-OH	H	H	β-OAc	Mycelia
86	3β,15α-Diacetoxylanosta-8,24-dien-26-oic acid	III	β-OAc	H	H	α-OAc	H	Mycelia
87	11α-Hydroxy-3,7-dioxo-5α-Lanosta-8,24(E)-dien-26-oic acid	III	O	O	α-OH	H	H	Fruit body
88	11β-Hydroxy-3,7-dioxo-5α-lanosta-8,24(E)-dien-26-oic acid	III	O	O	β-OH	H	H	Fruit body
89	Ganoderic acid LM2	IV	O	β-OH	H	O	OH	Fruit body
90	Ganoderic acid γ	IV	O	β-OH	H	α-OH	β-OH	Spore
91	Ganoderic acid δ	IV	O	α-OH	H	α-OH	β-OH	Spore
92	Ganoderic acid ε	IV	β-OH	β-OH	H	O	β-OH	Spore
93	Ganoderic acid ζ	IV	β-OH	O	H	O	β-OH	Spore
94	Ganoderic acid η	IV	β-OH	β-OH	β-OH	O	β-OH	Spore
95	Ganoderic acid θ	IV	β-OH	O	β-OH	O	β-OH	Spore
96	Ganolucidic acid D	IV	O	H	H	α-OH	β-OH	Spore/fruit body
97	Ganolucidic acid E	IV	O	H	H	α-OH	H	Fruit body
98	23S-Hydroxy-3,7,11,15-tetraoxolanost-8,24E-diene-26-oic acid		β-OH	O	O	O	H	Fruit body
99	Methyl ganoderate A		O	β-OH	H	α-OH	Me	Fruit body
100	Methyl ganoderate B	IV	β-OH	β-OH	H	O	Me	Fruit body
101	Methyl ganoderate D	V	O	β-OH	H	O	Me	Fruit body
102	Methyl ganoderate E	V	O	O	H	O	Me	Fruit body
103	Methyl ganoderate F	V	O	O	β-OAc	O	Me	Fruit body

Table 2 *Ganoderma* triterpenoids in *G. lucidum (Continued)*

No.	Compound name	Types	R_1	R_2	R_3	R_4	R_5	Source
104	Methyl ganoderate H	V	β-OH	O	β-OAc	O	Me	Fruit body
105	Methyl ganoderate J	V	O	O	H	α-OH	Me	Fruit body
106	Methyl-O-acetylganoderate C	V	β-OAc	O	β-OAc	O	Me	Mycelia
107	3β,7β-Dihydroxy-12β-acetoxy-11,15,23-trioxo-5α-lanosta-8-en-26-oic acid methyl ester	V	β-OH	β-OH	β-OAc	O	Me	Fruit body
108	Ethyl ganoderate J		O	O	H	α-OH	Et	Mycelia
109	Ethyl 3-O-Acetylganoderate B	V	β-OAc	β-OH	H	O	Et	Mycelia
110	12β-Acetoxy-3,7,11,15,23-pentaoxo-5α-lanosta-8-en-26-oic acid ethyl ester		O	O	β-OAc	O	Et	Fruit body
111	Butyl ganoderate A		O	β-OH	H	α-OH	Bu	Fruit body
112	Butyl ganoderate B	V	β-OH	β-OH	H	O	Bu	Fruit body
113	Butyl ganoderate H	V	β-OH	O	β-OAc	O	Bu	Fruit body
114	n-Butyl ganoderate H	V	β-OH	O	β-OAc	O	Bu	Fruit body
115	12β-Acetoxy-3β,7β-dihydroxy-11,15,23-trioxolanost-8-en-26-oic acid butyl ester		β-OH	β-OH	β-OAc	O	Bu	Fruit body
116	12β-Acetoxy-3,7,11,15,23-pentaoxolanost-8-en-26-oic acid butyl ester		O	O	β-OAc	O	Bu	Fruit body
117	Methyl ganoderate C1	V	O	β-OH	H	O	CH_3	Fruit body
118	Compound B8	V	O	OH	H	OH	H	Fruit body
119	Compound B9	V	β-OH	OH	H	OH	H	Fruit body
120	Methyl ganoderate M	V	O	β-OH	α-OH	O	O	Fruit body
121	Methyl ganoderate N	V	O	β-OH	H	O	OH	Fruit body
122	Methyl ganoderate K		β-OH	O	H	α-OH	H	Fruit body
123	Methyl ganoderate G		OH	OH	OH	O	H	*G. lucidum*
124	Methyl ganoderenate E	V	O	O	H	O	H	Fruit body
125	Methyl ganoderate I		OH	OH	H	O	OH	*G. lucidum*
126	Methyl ganoderate A		O	H	H	β-OH	H	Fruit body
127	Methyl ganoderate B	V	β-OH	H	H	α-OH	H	Fruit body
128	Ganoderal B	V	O	α-OH	H	H	CHO	Fruit body
129	Lucidadiol	V	OH	O	H	H	OH	Fruit body
130	Lucidal	V	β-OH	O	H	H	CHO	Fruit body
131	Lucialdehyde B	VI	O	O	H	H	CHO	Fruit body
132	Lucialdehyde E	VI	O	β-OH	O	α-OH	CHO	Spore
133	Lucialdehyde D	VI	O	O	O	H	CHO	Spore
134	Ganoderic aldehyde A	VI	O	β-OH	O	α-OH	CHO	Fruit body
135	Lucialdehyde C	VI	β-OH	O	H	H	CHO	Fruit body

peroxidation and decreasing the expression of inflammatory mediators.

Hypoglycemic effect

In recent years, the antidiabetic components and hypoglycemic mechanisms of *G. lucidum* have been studied. Protein tyrosine phosphatase 1B (PTP1B) is a therapeutic target in diabetes. A novel proteoglycan, called Fudan-Yueyang-*G. lucidum* (FYGL), has been extracted from *G. lucidum*. FYGL has dose-dependent hypoglycemic and hypolipidemic effects and could increase blood insulin levels. Furthermore, it inhibited the

Table 3 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	R_1	R_2	R_3	R_4	Source
146	Lucidenic acid A (lucidenate A)	VIII	O	β-OH	H	H	Fruit body
147	Lucidenic acid B	VIII	O	β-OH	β-OH	H	Fruit body
148	3β-Oxo-formyl-7β,12β-dihydroxy-4,4,14α-trimethyl-5α-chol-11,15-dioxo-8-en(E)-24-oic acid	VIII	β-OCHO	β-OH	OH	H	Fruit body
149	Lucidenic acid C	VIII	β-OH	β-OH	β-OH	H	Fruit body
150	Lucidenic acid D	VIII	O	O	β-OAc	H	Fruit body
151	Lucidenic acid D1	VIII	O	O	O	H	Fruit body
152	Lucidenic acid D2	VIII	O	O	β-OAc	H	Fruit body
153	Lucidenic acid E	VIII	β-OH	O	β-OAc	H	Fruit body
154	Lucidenic acid E1	VIII	O	β-OH	α-OH	H	Fruit body
155	Lucidenic acid E2	VIII	β-OH	O	β-OAc	H	Fruit body
156	Lucidenic acid F	VIII	O	O	H	H	Fruit body
157	Lucidenic acid N	VIII	β-OH	β-OH	H	H	Fruit body
158	Lucidenic acid P	VIII	β-OH	β-OH	β-OAc	H	Fruit body
159	20-Hydroxylucidenic acid D2	VIII	O	O	β-OAc	ξ-OH	Fruit body
160	20-Hydroxylucidenic acid E2	VIII	β-OH	O	β-OAc	ξ-OH	Fruit body
161	20-Hydroxylucidenic acid F	VIII	O	O	H	ξ-OH	Fruit body
162	20-Hydroxylucidenic acid N	VIII	β-OH	β-OH	H	ξ-OH	Fruit body
163	20-Hydroxylucidenic acid P	VIII	β-OH	β-OH	β-OAc	ξ-OH	Fruit body
164	3β-Hydroxy-4,4,14-trimethyl-7,11,15-trioxochol-8-en-24-oic acid	VIII	β-OH	O	H	H	Fruit body
165	Ganoderal A	IX	O	H	Me	CHO	Fruit body
166	Lucialdehyde A	IX	β-OH	H	Me	CHO	Fruit body
167	Ganoderic aldehyde TR	IX	O	α-OH	CHO	Me	Fruit body
168	Ganoderol A(ganodermenonol)	IX	O	H	Me	CH2OH	Fruit body
169	Ganoderol B	IX	β-OH	H	Me	CH2OH	Fruit body/ mycelia
170	Ganodermatriol	IX	β-OH	H	CH2OH	CH2OH	Fruit body
171	Ganoderiol B	IX	O	α-OH	CH2OH	CH2OH	Fruit body
172	Ganoderiol F	IX	O	H	CH2OH	CH2OH	Fruit body
173	5α-Lanosta-7,9(11),24-triene-15α-26-dihydroxy-3-one	IX	O	α-OH	Me	CH2OH	Fruit body
174	Lucidenic acid O	XI	β-OH	OH	α-OH	H	Fruit body
175	20(21)-Dehydrolucidenic acid A	XI	O	H	O	H	Fruit body
176	Methyl 20(21)-dehydrolucidenate A	XI	O	H	O	Me	Fruit body
136	Ganoderenic acid A	X	O	β-OH	H	α-OH	Fruit body
137	Ganoderenic acid B	X	β-OH	β-OH	H	O	Fruit body
138	Ganoderenic acid C	X	β-OH	β-OH	H	α-OH	Fruit body

Table 3 *Ganoderma* triterpenoids in *G. lucidum (Continued)*

No.	Compound name	Types	R_1	R_2	R_3	R_4	Source
139	Ganoderenic acid D	X	O	β-OH	H	O	Fruit body
140	Ganoderenic acid K	X	β-OH	β-OH	β-OAc	O	Fruit body
141	Ganoderenic acid E	X	O	β-OH	β-OH	O	Gill
142	Elfvingic acid A	X	O	O	α-OH	β-OH	Fruit body
143	12β-Acetoxy-7β-hydroxy-3,11,15,23-tetraoxo-5α-lanosta-8,20-dien-26-oic acid	X	O	β-OH	β-OAc	O	Fruit body
144	12β-Acetoxy-3β-hydroxy-7,11,15,23-tetraoxo-lanost-8,20E-diene-26-oic acid	X	β-OH	O	β-OAc	O	Fruit body
145	12β-Acetoxy-3β,7β-dihydroxy-11,15,23-trioxo-5α-lanosta-8,20-dien-26-oic acid	X	β-OH	β-OH	β-OAc	O	Fruit body

overexpression of PTP1B, enhanced insulin-stimulated glycogen synthesis, and decreased blood glucose in a mouse model of insulin resistance (Tian et al. 2018). FYGL can ameliorate type 2 diabetes mellitus caused by mitochondrial dysfunction and can decrease ROS level (Yang et al. 2019).

In addition, GLPs can downregulate the activity of hepatic glucose-regulated enzymes and epididymal fat/BW ratio and improvement of insulin resistance (Xiao et al. 2017). The results demonstrated that GLPs have significant hypoglycemic properties and that it may be an effective dietary food for the prevention and treatment of obesity and diabetes.

Anti-inflammatory effect

Inflammation is a normal physiological response to an infection or injury, which is part of host defense and tissue healing (Lee and Choi 2018). In the inflammatory environment of the body, elevated levels of TNF-α, IFN-γ, and IL-4 can further accelerate the inflammatory response in the dermis and destroy epidermal barrier function. GLPss58, a sulfated form of a polysaccharide from the fruiting body of *G. lucidum*, can inhibit the binding of L-selectin with the receptor, activate the complement systems, and block the binding of TNF-α and INF-γ to their antibodies. GLPss58 could inhibit all the L-selectin-, complement-, and cytokine-mediated inflammation pathways (Zhang et al. 2018a, 2018b). In addition, GLPs can prevent inflammation, maintain intestinal homeostasis, and regulated the intestinal immunological barrier functions in mice by markedly suppressing the secretions of TNF-α, IL-1β, IL-6, and IL-4 (Wei et al. 2018). The anti-inflammatory effect of GLPs plays an important role in clinic for sensitive skin.

Effect on the skin

G. lucidum has been an important functional ingredient in many salve formulations due to its anti-aging, anti-melanogenesis, and skin barrier-enhancing properties.

Anti-melanogenesis effects

The abnormal accumulation of melanin causes skin pigmentation. Tyrosinase is an enzyme that regulates melanin synthesis. *G. lucidum* can inhibit the activity of tyrosinase and tyrosine-related proteins, which prevents hyperpigmentation. Methyl lucidenate F isolated from *G. lucidum* showed a dose-dependent tyrosinase inhibitory activity, with an IC_{50} of 32.23 μM (Zhang et al. 2011). On the other hand, the cAMP-dependent signaling pathway regulates melanogenesis by inhibiting cellular phosphorylation of the cAMP-responsive element-binding protein (CREB). Thus, downregulating the expression of microphthalmia-associated transcription factor (MITF) decreases melanin production (Liu et al. 2015). The active compound *Ganoderma* mannitol was obtained from *G. lucidum*. Compared to arbutin (0.5 mM), ganodermanondiol (10 μM) significantly reduced the melanin content in B16F10 melanoma cells. Furthermore, the inhibitory effect of ganodermanondiol contributed to the reduction in MITF expression and melanin production through the inhibition of CREB phosphorylation. The phosphorylation of extracellular regulated protein kinase (ERK) and c-Jun N-terminal kinase (JNK) downregulated melanin synthesis, but phosphorylation of p38 triggered MITF expression and melanin production. Ganodermanondiol induced the phosphorylation of ERK and JNK suppressed the phosphorylation of p38 (Kim et al. 2016). GLPs are different from GTs in that they can directly affect melanogenesis in melanocytes. GLP can antagonize UVB-induced skin pigmentation in vivo (Hu et al. 2019a, 2019b). GLP can inhibit the paracrine effects of keratinocytes and fibroblasts via the fibroblast growth factor (FGF2)/MAPK pathway to decrease melanogenesis in melanocytes (Jiang et al. 2019). *G. lucidum* can treat pigmentary dermatosis such as solar lentigo, chloasma, freckles, and senile plaques.

Antioxidant and anti-aging activity

UV is a primary environmental factor implicated in skin aging; it causes coarse wrinkling, dryness, and laxity

Table 4 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	R_1	R_2	R_3	Source
177	Ganoderic acid P	XII	α-OH	α-OAc	β-OAc	Mycelia
178	Ganoderic acid Q	XII	α-OAc	α-OH	β-OAc	Mycelia
179	Ganoderic acid R	XII	α-OAc	H	β-OAc	Fruit body /mycelia
180	Ganoderic acid S	XII	α-OH	H	β-OAc	Mycelia
181	Ganoderic acid T	XII	α-OAc	α-OAc	β-OAc	Fruit body /mycelia
182	Ganoderic acid Y	XII	β-OH	H	H	Fruit body
183	Ganoderic acid X	XII	α-OH	α-OAc	H	Mycelia
184	Ganoderic acid TR1	XII	O	β-OH	H	Fruit body
185	Ganoderic acid Me	XII	α-OAc	α-OAc	H	Fruit body /mycelia
186	Ganoderic acid Mf	XII	α-OAc	α-OH	H	Fruit body /mycelia
187	15-Hydroxy ganoderic acid S	XII	O	α-OH	H	Fruit body
188	Ganodermic acid S	XII	β-OAc	α-OAc	H	Fruit body
189	Ganodermic acid Ja	XII	α-OH	α-OH	H	Mycelia
190	Ganodermic acid Jb	XII	β-OH	α-OH	H	Mycelia
191	Ganodermic acid R	XII	α-OAc	α-OAc	H	Mycelia
192	Ganodermic acid P1	XII	α-OAc	α-OH	OAc	Mycelia
193	Ganodermic acid P2	XII	β-OH	α-OAc	β-OAc	Mycelia
194	Ganodermic acid T-N	XII	β-OH	α-OAc	H	Mycelia
195	Ganodermic acid T-O	XII	β-OAc	α-OH	H	Fruit body
196	Ganodermic acid T–Q	XII	O	α-OAc	H	Mycelia
197	3α,15α,22α-Trihydroxylanosta-7,9(11),24-trien-26-oic acid	XII	α-OH	α-OH	α-OH	Mycelia
198	3α,15α-Diacetoxy-22α-hydroxylanosta-7,9(11),24-trien-26-oic acid	XII	α-OAc	α-OAc	α-OH	Mycelia
199	3β,15α-Diacetoxy-22α-hydroxylanosta-7,9(11),24-trien-26-oic acid	XII	β-OAc	α-OAc	α-OH	Mycelia
200	3β,15α,22β-Trihydroxylanosta-7,9(11),24-trien-26-oic acid(ganodermic acid S)	XII	β-OH	α-OH	β-OH	Mycelia
201	22β-Acetoxy-3α,15α-dihydroxylanosta-7,9(11),24-trien-26-oic acid	XII	α-OH	α-OH	β-OAc	Mycelia
202	22β-Acetoxy-3β,15α-dihydroxylanosta-7,9(11),24-trien-26-oic acid	XII	β-OH	α-OH	β-OAc	Mycelia
203	Lanosta-7,9(11),24-trien-3α-acetoxy-15α,22β-dihydroxy-26-oic acid	XII	α-OAc	α-OH	β-OH	Fruit body
204	Lanosta-7,9(11),24-trien-3β,15α,22β-triacetoxy-26-oic acid	XII	β-OAc	α-OAc	β-OAc	Fruit body
205	Lanosta-7,9(11),24-trien-3α-acetoxy-15α-hydroxy-23-oxo-26-oic acid	XIII	α-OAc	OH	O	*G. lucidum*
206	Lanosta-7,9(11),24-trien-15α-acetoxy-3α-hydroxy-23-oxo-26-oic acid	XIII	α-OH	OAc	O	*G. lucidum*
207	Lanosta-7,9(11),24-trien-3α,l5α-diacetoxy-23-oxo-26-oic acid	XIII	α-OAc	OAc	O	*G. lucidum*
208	Ganoderic acid Sz	XIV	O	H	H	Fruit body
209	Ganoderic acid TR	XIV	O	α-OH	H	Fruit body
210	23-Hydroxy ganoderic acid S	XIV	OH	H	OH	Fruit body
211	Lucidone A	XV	β-OH	β-OH	O	Fruit body
212	Lucidone B	XV	O	β-OH	O	Fruit body
213	Lucidone C	XV	β-OH	β-OH	α-OH	Fruit body
214	Ganoderiol E (3β, 26,27-trihydroxy-5α-lanosta-8,24-dien-7-one)	XVI	β-OH	O	H	Fruit body
215	Ganoderiol I (15α, 26,27-trihydroxy-5α-lanosta-8,24-dien-3-one)	XVI	O	α-OMe	α-OH	Fruit body
216	Methyl Ganolucidate C	XVII	OH	OH	Me	Fruit body
217	Ganolucidic acid C	XVII	OH	OH	H	Fruit body
218	methyl ganolucidate B	XVII	OH	H	Me	Fruit body
219	methyl lucidenate G	XXVII	O	OH	CH_3	Fruit body
220	Lucidenic acid G	XXVII	O	OH	H	Fruit body

Table 5 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	*R*	Source
221	Ganosporelactone A	XVIII	O	Spore
222	Ganosporelactone B	XVIII	OH	Spore
223	Epoxyganoderiol B	XIX	O	Fruit body
224	Epoxyganoderiol C	XIX	β-OH	Fruit body
225	26-Hydroxy-5α-lanosta-7,9(11),24-triene-3,22-dione	XX	Me	Fruit body
226	26,27-Dihydroxy-5α-lanosta-7,9(11),24-triene-3,22-dione	XX	CH2OH	Fruit body
227	Ganoderitriol M	XXI	β-OH	Fruit body
228	Lucidumol A	XXI	O	Fruit body/spore
229	Ganodermanondiol	XXII	O	Fruit body/spore
230	Lucidumol B	XXII	β-OH	Fruit body/spore

(Kong et al. 2018). UVB irradiation stimulates MMP-1 secretion and reduces the synthesis of collagen and elastin, which can accelerate skin senescence (Hwang et al. 2018). The extract of *G. lucidum* can inhibit UVB-induced MMP-1 expression and increased procollagen expression by inhibiting ERK pathways (Lee et al. 2018). GLPs can inhibit MMP-1 protein expression, promote C-telopeptides of type I collagen protein, and inhibit ROS production in fibroblasts following UVB treatment (Zeng et al. 2017).

The long-term presence of free radicals and ROS accelerates aging and numerous age-associated illnesses (Bishop et al. 2015). Therefore, studies on scavenging free radicals and ROS are particularly important in anti-aging research.

The antioxidant properties of crude proteins obtained from the mycelium and fruiting bodies of *G. lucidum* were studied. It was found that protein from both the mycelia and fruit body exhibited antioxidant capacity. The mycelial protein extract showed better scavenging activities than those shown by fruiting body protein extract, in terms of both 2,2′-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) radical- and 2,2-diphenylpicrylhydrazyl radical (DPPH•) radical-scavenging abilities (Sa-Ard et al. 2015). Oxidative stress markers were measured by using the comet assay to measure ROS generation. Furthermore, the ethanol extract of *G. lucidum* could significantly reduce H_2O_2-induced ROS production compared to that in the positive control (Lee et al. 2016).

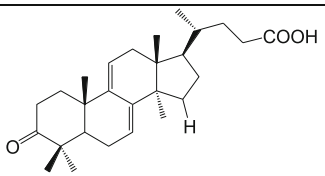
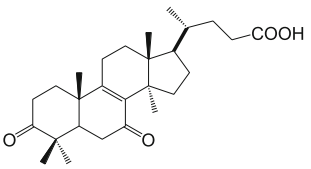
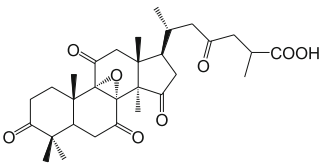
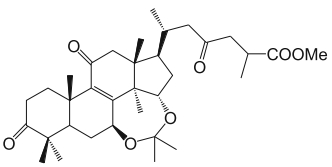
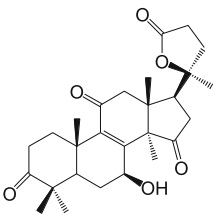
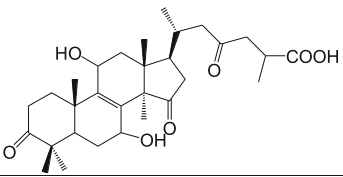
Skin barrier-repairing activity

A wound damages the skin barrier, which will cause microbial invasion and inflammation. *G. lucidum*, as a wound-healing agent, can be used to treat chronic non-healing wounds in vitro (Montalbano 2018). Nanogel containing triterpenoids isolated from *G. lucidum* has shown beneficial effects on the frostbite healing process by increasing the wound healing area and improving the degree of pathological change in skin tissue of rats with frostbite (Shen et al. 2016). GLP promotes the migration ability of fibroblasts and upregulates the expressions of C-terminal peptide of procollagen type I and transforming growth factor-β1 in fibroblasts, so it can heal wounds

Table 6 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound name	Types	R_1	R_2	Source
231	Ganoderiol C	XXIII	O	α-OEt	Fruit body
232	Ganoderiol D	XXIII	O	O	Fruit body
233	Ganoderiol G	XXIII	O	α-OMe	Fruit body
234	Ganoderiol H	XXIII	β-OH	O	Fruit body
231	Ganodermanontriol	XXIV	O	α-OH	Fruit body/spore
232	Ganoderiol A	XXIV	β-OH	OH	Fruit body
233	8β,9α-Dihydroganoderic acid C	XXV	H	O	Mycelia
234	8β,9α-Dihydroganoderic acid J	XXV	H	α-OH	Fruit body
235	Ganosporeric acid A	XXV	O	O	Spore
236	3β,7β-Dihydroxy-11,15,23-trioxo-lanost-8,16-dien-26-oic acid	XXVI	H	O	Fruit body
237	12β-Acetoxy-3β,7β-dihydroxy-11,15,23-trioxo-lanost-8,16-dien-26-oic acid	XXVI	β-OAc	O	Fruit body

Table 7 *Ganoderma* triterpenoids in *G. lucidum*

No.	Compound Name	Structures of compounds	Source
238	4,4,14α-trimethyl-5α-chol-7,9(11)-dien-3-oxo-24-oic acid		fruit body
239	4,4,14α-Trimethyl-3,7-dioxo-5α-chol-8-en-24-oic acid		fruit body
240	8α,9α-Epoxy-3,7,11,15,23-pentaoxo-5α-lanosta-26-oic acid		fruit body
241	Methyl ganoderate A acetonide		fruit body
242	Lucidenolactone		fruit body
243	Ganoderic acid Df		fruit body

(Hu et al. 2019a, 2019b). Thus, *G. lucidum* can be used for barrier repair to promote wound regeneration.

Other effects

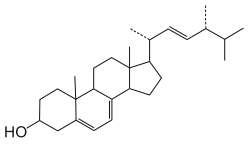
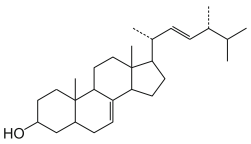
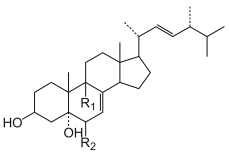
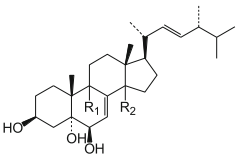
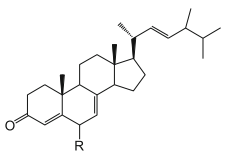
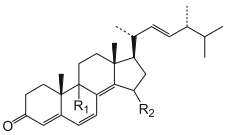
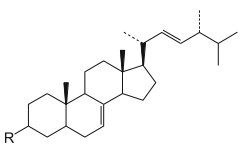
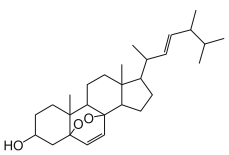
Besides the above-mentioned pharmacological actions, the extract of *G. lucidum* can activate the AMPK/mTOR and PINK1/Parkin signaling pathways and regulate mitochondrial function, autophagy, and apoptosis, thus improving parkinsonian symptoms (Ren et al. 2018). *G. lucidum* can induce the secretion of immunoglobulin A and ameliorate intestinal infections (Kubota et al. 2018).

In summary, the anticancer and anti-inflammatory effects of *G. lucidum* have been confirmed in cell assays and signaling pathways, and especially, hypoglycemic effects have been demonstrated in mice. However, *G. lucidum* effects have been investigated in few clinical trials in humans. Therefore, the side effects of *G. lucidum* need to be further studied. Further, the melanin inhibitory, anti-aging, antioxidant, and skin barrier-enhancing properties of the secondary metabolites from *G. lucidum* should be focused on more in future research. *G. lucidum* has great potential in the development of medicines, cosmeceuticals, and nutritional supplements and the research and development of *G. lucidum* resources are of great significance.

Conclusions

G. lucidum is a traditional Chinese medicine that has been used for centuries as a nutritional supplement and herbal medication. This review summarizes the active substances of *G. lucidum*. Polysaccharides and triterpenoids are the major secondary metabolites of *G.*

Table 8 Steroids in *G. lucidum*

No.	Compound Name	Structures of compounds	R	Source
244	Ergosterol			fruit body/ spore
245	stellasterol			spore
246	3β,5α-Dihydroxy-6β-methoxy ergosta-7,22-diene		R1= H R2= β-OMe	fruit body
247	6-dehydrocerevisterol		R1= H R2= O	spore
248	3β,5α,9α-Trihydroxy-(22E,24R)-ergosta-7,22-dien-6-one		R1= α-OH R2= O	spore
249	22E,24R-Ergosta-7,22-diene-3β,5α,6β-triol		R1 = H R2= H	spore
250	22E,24R-Ergosta-7,22-diene-3β,5α,6β,9α-tetraol		R1 = α-OH R2 = H	spore
251	22E,24R-Ergosta-7,22-diene-3β,5α,6β,9α,14a-pentol		R1 = α-OH R2 = α-OH	spore
252	6α-Hydroxy-ergosta-4,7,22-trien-3-one		R=α-OH	fruit body
253	6β-Hydroxy-ergosta-4,7,22-trien-3-one		R=β-OH	fruit body
254	Ergosta-4,7,22-triene-3,6-dione		R=O	mycelium
255	Ganodermaside A		R1= H R2= α-OH	spore
256	Ganodermaside B		R1= H R2= β-OH	spore
257	Ganodermaside C		R1=α-OH R2= O	spore
258	Ganodermaside D		R1=α-OH R2= H	spore
259	Ergosta-7,22-dien-3-one		R=O	fruit body
260	Ergosta-7,22-diene-3β-yl pentadecanoate		R=β-O-pentadecanoyl	fruit body
261	Ergosta-7,22-dien-3β-yl palmitate		R=β-O-palmitoyl	fruit body
262	Ergosta-7,22-dien-3β-yl linoleate		R=β-O-linoleoyl	fruit body
263	5α,8α-epidioxyergosta-6,22-dien-3β-ol			fruit body

lucidum. The polysaccharides mostly comprise α- or β-(1→3)-, (1→6)-glucans and hetero-polysaccharides. More than 200 kinds of GTs have been isolated from *G. lucidum*. GTs can effectively inhibit the proliferation and metastasis of cancer cells. Ganoderic acids are the prominent bioactive constituents of GTs. Ganoderic acid A, ganoderic acid F, ganoderic acid H, ganoderic acid C, ganoderic acid D, ganoderic acid T, ganoderic acid X, and ganoderic acid Y can be used as adjuvant drugs to suppress cancer. Therefore, the application of GTs in the pharmaceutical industry is very important.

In addition, the secondary metabolites isolated from *G. lucidum* can be used in functional foods or medicines for properties such as anti-aging, decreased surface pigmentation, and skin barrier-enhancing effects. GTs, especially methyl aspartate and *Ganoderma* mannitol, have skin-whitening effects. Crude proteins obtained from the mycelia and fruiting bodies of *G. lucidum* show antioxidant effects. GLPs can inhibit the expression of MMP-1, increase procollagen expression, and scavenge free radicals and reactive oxygen species, which can delay aging. The human internal environment is interacted by many kinds of cells through various forms. Although the pharmacological effects of *G. lucidum* have been confirmed at the level of monolayer cells, monolayer cells can not simulate the multicellular environment in vivo, so the effect of *G. lucidum* on multicellular interconnection can not be explored. We can use cell co-culture to study the relationship between different cells in order to verify the pharmacological effect of *G. lucidum*.

In recent years, with the development of microbial technology, it has a good prospect to obtain GTs through microbial fermentation technology. *G. lucidum* has become a popular nutraceutical worldwide; it has great cosmeceutical potential. *G. lucidum*, as a good medicinal and food homologous medicinal material, has received more and more attention in the food health care and cosmetics industry, and its application in food health products and cosmetics has potential for further exploration.

Abbreviations

AMPK: AMP-activated protein kinase; Bcl-2: B cell lymphoma-2; Bcl-xL: B cell lymphoma-extra large; cAMP: Cyclic adenosine monophosphate; CREB: cAMP-responsive element-binding protein; ERK: Extracellular signal regulated kinase; FGF2: Fibroblast growth factor; *G. lucidum*: *Ganoderma lucidum*; GLE: Extract of *G. lucidum*; GLPs: *G. lucidum* polysaccharides; Il-2: Serum interleukin-2; INF-γ: Interferon-γ; JNK: c-Jun N-terminal kinase; LZ-8: Ling Zhi-8; MAPK: Mitogen-activated protein kinase; MITF: Microphthalmia-associated transcription factor; MMP: Matrix metalloproteinase; ROS: Reactive oxygen species; SOD: Superoxide dismutase; t-BHP: Tertbutyl hydrogenperoxide; TNF-α: Tumor necrosis factor-α; UV: Ultraviolet; UVB: Ultraviolet B

Acknowledgements

This work was supported by China Cosmetic Collaborative Innovation Center, the Open Research Fund Program of Beijing Key Lab of Plant Resource Research and Development, BTBU(PRRD-2017-ZD1).

Authors' contributions

LL and FY designed and finalized the scheme; YLY performed the review work and wrote the paper; JHZ drawn some structural formulas; WSZ, XYG, and HNZ contributed to the manuscript writing. All authors read and approved the final manuscript.

Funding

This work was supported by China Cosmetic Collaborative Innovation Center, the Open Research Fund Program of Beijing Key Lab of Plant Resource Research and Development, BTBU(PRRD-2017-ZD1).

Availability of data and materials

Not applicable

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Received: 23 July 2019 Accepted: 20 September 2019
Published online: 29 November 2019

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