Current and future perspective on antimicrobial and anti-parasitic activities of *Ganoderma* sp.: an update

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**ABSTRACT**

Medicinal mushroom *Ganoderma* sp. is considered to be a key source for the production of therapeutic agents. Our current review indicates that a limited number (<19%; 79 out of >430) of isolated compounds have been tested and known to be active against several microorganisms and parasites. In this review, we aim to summarise all the antimicrobial and anti-parasitic works on *Ganoderma* sp. displayed on web of science, google scholar and endnote X7 from 1932 to August 2016. We further present and discuss the structure of active compounds against microorganisms and parasites. In addition, we also discuss the possible further research to identify lead compounds from *Ganoderma* sp. as a novel strategy to combat the potential global emergence of bad bugs and parasites.

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**1. Introduction**

*Ganoderma* sp. is a medicinal mushroom producing a group of frequently studied bioactive compounds. They belong to the kingdom of Fungi, division of Basidiomycota, class of Agaricomycetes, order Polyporales, family of Ganodermataceae and genus of Ganoderma. A search for “Ganoderma” in the database Index Fungorum displayed 409 species records, including synonyms ([http://www.speciesfungorum.org](http://www.speciesfungorum.org)). *Ganoderma* sp., especially *G. lucidum*, *G. tsugae* and *G. applanatum*, are well studied and have been in use in East Asian countries since the ancient times for the treatment of various diseases (Ofodile et al. 2005; Paterson 2006; Ferreira et al. 2015). Triterpenes and polysaccharides are considered key constituents isolated from fruiting bodies, gills, spores and mycelia for their bioactivities (Xia et al. 2014).

Literature reviews suggest, besides its antimicrobial activities, *Ganoderma* sp. components exhibit a variety of bioactivities, including anti-tumour, immune-modulatory, antioxidant, anti-hypertensive and anti-androgenic. Moreover, *Ganoderma* sp. is widely used for the remedy of various chronic diseases such as cancers, diabetes, hypertension and hepatitis (Ofodile et al. 2005; Zhang et al. 2015). To date, most of the reviews on *Ganoderma* sp. have been focused on its anticancer and antioxidant activities and immune modulation (Sanodiya et al. 2009). Therefore, our basic aim is to provide a glimpse on the antimicrobial and anti-parasitic activities of *Ganoderma* sp. In addition, we also provide possible future prospect for research on *Ganoderma* sp. and its compounds.

In this review, we have performed literature searches in English (ISI Web of Science and Google Scholar) and Endnote X7 (online search, Pub Med) to find publications that described *Ganoderma* sp. for antimicrobial activities. We have used the keywords “Ganoderma” and “Antimicrobial”. Finally, we filtered individual references to determine the relevancy to our study. The inclusion criterion was the study that provided data or results or discussion on the antimicrobial activities of *Ganoderma* sp.

**2. Antimicrobial and anti-parasitic bioactive compounds**

*Ganoderma* sp. has been reported as important sources of antimicrobial bioactive compounds. Terpenes, terpenoids and polyketides of farnesyl quinones types are the major secondary metabolites
(SMs) produced by *Ganoderma* sp. In *Ganoderma* sp., more than 316 terpenes have been reported, with the majority of compounds from *G. lucidium* (Xia et al. 2014).

Chemical analysis of numerous *Ganoderma* sp. has showed *Ganoderma* Triterpenes (GTs) are mainly lanostanoid-type triterpene (Zhang et al. 2015). Among them, majority contain 30 or 27 carbon atoms, and some occasionally may contain 24 carbon atoms. These compounds possess the same parent skeleton, namely a trans-configuration of rings A/B, B/C, C/D and 10β, 13β, 14α, 17β substituent. In addition, the substituents are always found at the C-3, 7, 11, 12, 15, 22, 23, 24 and 25 positions of the parent nucleus (Xia et al. 2014). Thirty carbon terpenoids are usually formed by the fusion of two smaller terpenoids precursors, each containing 15 carbons sesquiterpene. Head-to-tail fashion linking of isoprene units to form linear chains and various cyclisations and rearrangements is the core mechanism to give cyclic terpenoids (Mothana et al. 2000; Hill & Connolly 2013). The parent carbon skeleton of antimicrobial and anti-parasitic GTs is shown in Figure 1, from which it can be concluded that GTs are the most common antimicrobial and anti-parasitic compounds reported from *Ganoderma* sp.

Farnesyl quinone, a polyketide type, is the second most common antimicrobial and anti-parasitic compound from *Ganoderma* sp. Quinones are known to be oxidised derivatives of aromatic compounds and are often readily made from reactive aromatic compounds with electron-donating substituent such as catechols and phenols. Besides GTs, polypeptides, small peptides such as ganodermin, polysaccharide such as sacchachitin, and chitosan also possess antimicrobial and anti-parasitic properties (Mothana et al. 2000; Wang & Ng 2006; Sanodiya et al. 2009; Chuang et al. 2013). Structures of antimicrobial and anti-parasitic compounds from *Ganoderma* sp. are shown in Figure 2.

### 3. Isolation of antimicrobial and anti-parasitic bioactive compounds

Extracts from fruiting bodies, both wild and cultivated, and mycelia from fermentation broth (Tables 1–4) are used for the isolation of antimicrobial and anti-parasitic bioactive compounds. Literatures divulge that most commonly ethanol (EtoAc) (Tables 1–4) is used to prepare crude extract; sometimes some researchers preferred other solvents such as chloroform (CHCl₃), EtOH, and acetone (Isaka et al. 2016). In addition, our review reveals that hexane and ether are poorly used for the preparation of extract from *Ganoderma* sp. Moreover, some techniques such as microwave, ultrasound and enzyme treatments can facilitate the breakdown of the cell wall (Ferreira et al. 2015). Solvents like MeOH, EtOH, CH₂Cl₂, CHCl₃ and aqueous – both cold and hot – are used for further purifications and isolation. Techniques such as thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), and column chromatography (CC) are used to facilitate the purification and isolation process (Huie & Di 2004). The general procedures of the isolation of antimicrobial and anti-parasitic compounds are shown in Figure 3. In addition, this outline can be used for other chemical investigations from *Ganoderma* sp.

**Figure 1.** Parent carbon skeletons of triterpenoid and farnesyl quinone type of polyketide from *Ganoderma* sp. with antimicrobial and anti-parasitic activities.
4. Antibacterial activities of compounds and extracts of *Ganoderma* sp

Currently bioassay-guided antibiotics identification, TLC and chromatography bio-autography are used to track antibacterial ingredients from the extract (Huie & Di 2004). Minimum inhibitory concentration (MIC) and 50% inhibitory concentration (IC<sub>50</sub>) values are used to determine the potency of antibacterial agents. Our literatures review showed that MeOH and EtOH are good solvents for the extraction of antibacterial compounds of interest rather than other organic solvents; however, the parts of *Ganoderma* sp. used and the tested bacterial strains may be the limiting factors in
choosing the solvent. Most studies that use alcoholic solvents for extraction showed very low MIC (Li et al. 2012; Shang et al. 2013; Cilerdzic et al. 2016). Several studies on the fruiting bodies of *Ganoderma* sp. reveal that the compounds have the inhibitory ability to the different types of Gram positive bacteria (GPB), Gram negative bacteria (GNB) including the mycobacteria (Al-Fatimi et al. 2005; Isaka et al. 2016).

Colossolactone E (6) and 23-hydroxycolossolactone E (53), two colossolactones-triterpenes, were active against *Bacillus subtilis* and *Pseudomonas syringae*. However, the researcher did not determine the MIC and MBC of compounds against this bacterium (Ofodile et al. 2011). Moreover, two hydroquinones, ganomycins A (27) and B (28), were found to be the most effective to inhibit the bacterium. The MIC values of compounds 27 and 28 were 25 µg/ml.
against *Staphylococcus aureus* and 2.5 µg/ml against *Micrococcus flavus*, respectively, taking positive control ampicillin (MIC = 0.05 µg/ml and 0.25 µg/ml for *S. aureus* and *M. flavus*, respectively). In addition, in agar diffusion assay Zone of Inhibition (ZOI) 15–25 mm/100 µg/paper disk was found for GPB such as *B. subtilis, S. aureus* and *M. flavus*. However, *P. aeruginosa, Candida albicans* and *C. maltose* at 100 µg/paper disk did not respond to these compounds (Mothana et al. 2000). In a work performed by Isaka et al. (2016), EtOAc and MeOH extract of *Ganoderma* sp. BCC 16,642 isolated different compounds astraodoric acid C (50), ganorbiformin F (72), ganoderic acid TR (34), ganoderic acid T (73), ganoderic acid S (18), lanostanoid, ((22S,24E)-3β,15α,22-triacetoxylanosta-8,24-dien-26-oic acid (45), (24E)-3β-acetoxy-7α-hydroxylanosta-8,24-dien-26-oic acid (44), (24E)-3β,15α-diace oxy-7α-hydroxylanosta-8,24-dien-26-oic acid (43), (22S,24E)-7α-hydroxy-3β,15α,22-triacetoxylanosta-8,24-dien-26-oic acid (42), (22S,24E)-3β,22-diacetoxy-7α-methoxy-8,24-dien-26-oic acid (46), (22S,24E)-7α-methoxy-3β,15α,22-triacetoxylanosta-8,24-dien-26-oic acid (47), (22S,24E)-3β,22-diacetoxylanosta-7,9(11),24-trien-26-oic acid (41), which were observed to be active against the *Tubercular bacilli* with the MIC value in the range of 0.781–50 µg/ml. In another study, steroidal compounds like ergosta-5,7,22-trien-3β-yl acetate (11), ergosta-5,7,22-dien-3β-yl acetate (70), ergosta-7,22-dien-3-one (15), ergosta-7,22-dien-3β-ol (13), ergosta-5,7,22-trien-3β-ol (12) and ganoderadiol (20) were found to be effective against *S. aureus* and *B. subtilis* with MIC value of 2.5–5 mg/ml (Vazirian et al. 2014). Ethanolic and EtOAc extract
compounds 12β-acetoxy-3β, 7β-dihydroxy-11, 15, 23-trioxolanost-8-en-26-oic acid butyl ester (71) from fruiting bodies of *G. lucidium* showed significant inhibition against *S. aureus* and *B. subtilis* with MIC values of 68.5 µM and 123.8 µM, respectively (positive control ampicillin = 4.1 µM and 19.3 µM, resp.) (Liu et al. 2014).

Literatures reveal most of the antibacterial tests are performed on crude extract with significant effective results rather than pure compounds (Sa-Ard et al. 2015; Zengin et al. 2015; Cilerdzic et al. 2016). In addition, scanty information is available on the in vivo model test of effective compounds; we noticed only compounds (27) and (28) have been tested the in vivo model of the Methicillin-resistant Staphylococcus aureus (MRSA)-infected mouse (Mikolasch et al. 2016).

5. **Antifungal activities of compounds and extracts of *Ganoderma* sp**

An antifungal protein – ganodermin – isolated from the fruiting bodies of *G. lucidium* inhibits the growth of *Botrytis cinerea, Fusarium oxysporum* and *Physalo..."
| Ganoderma sp. | Extraction Solvent | Parts/products/compounds | Tested bacteria strains | Method | MIC/MBC | References |
|--------------|-------------------|--------------------------|-------------------------|--------|---------|-----------|
| *G. atrum*   | EtOH soluble acidic components | Fruiting bodies | *S. aureus* sub species Aureus, *E. coli*, *B. subtilis*, *P. vulgaris* | Micro dilution | 1.56-25mg/ml/3.125-25mg/ml | (Li et al. 2012) |
| *G. lucidum* | 96% EtOH | Fruiting bodies | *H. pylori* ATCC 43504, *S. aureus* ATCC 26003 | Micro plate Agar, Disc fusion Assay | ND | (Shang et al. 2013) |
| *G. colossum* | Hexane: CH$_2$Cl$_2$ (2:7) | Collosolactone E(6), 23 hydroxycollosolactone E(53) | *B. subtilis* IMI 347329, *P. syringae* var IMI 34748(ACTCC 19310) | TLC Agar Overlay | ND | (Laureta Nawannaka Ofoide et al. 2011) |
| *G. pfeifferi* | CH$_2$Cl$_2$ | Ganomycins A-B(27–28) | *S. aureus* (ATCC 6538), *B. subtilis* (SBUG 14), *E. coli* (SBUG 13), *P. mirabilis* (SBUG 47), *S. marcescens* (SBUG 9), *M. flavus* (SBUG 16) | Micro dilution | 2.5-25µg/ml/ND | (Mohtama et al. 2000) |
| *G. applanatum* | 96% EtOH | Mycelia extract | *B. cereus* (clinical isolate), *M. flavus* ATCC 10240, *S. aureus* ATCC 6538, *L. monocytogenes* NCTC 9793, *E. coli* ATCC 35218, *E. cloacae* (human isolate), *P. aeruginosa* ATCC 27853 and *S. typhimurium* ATCC 13311 | Micro dilution | 4.00mg/ml/1.25-25mg/ml | (Cilerdzic et al. 2016) |
| *G. carnosum* | 96% EtOH | Mycelia extract | *B. cereus* (clinical isolate), *M. flavus* ATCC 10240, *S. aureus* ATCC 6538, *L. monocytogenes* NCTC 9793, *E. coli* ATCC 35218, *E. cloacae* (human isolate), *P. aeruginosa* ATCC 27853 and *S. typhimurium* ATCC 13311 | Micro dilution | 4.00mg/ml/1.25-25mg/ml | (Cilerdzic et al. 2016) |
| *G. lucidum* | 96% EtOH | Mycelia extract | *B. cereus* (clinical isolate), *M. flavus* ATCC 10240, *S. aureus* ATCC 6538, *L. monocytogenes* NCTC 9793, *E. coli* ATCC 35218, *E. cloacae* (human isolate), *P. aeruginosa* ATCC 27853 and *S. typhimurium* ATCC 13311 | Micro dilution | 1.00-1.67mg/ml/1.16-400mg/ml | (Cilerdzic et al. 2016) |
| *G. colossum* | CH$_2$Cl$_2$, MeOH, H$_2$O | Fruiting bodies | *S. aureus* (ATCC 29213), *B. subtilis* (ATCC 6059), *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853), *M. flavus* (SBUG 16) | Micro dilution | 4.00mg/ml/1.25-25mg/ml | (Al-Fatimi et al. 2005) |
| *G. resinaceum* | CH$_2$Cl$_2$, MeOH, H$_2$O | Fruiting bodies | *S. aureus* (ATCC 29213), *B. subtilis* (ATCC 6059), *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853), *M. flavus* (SBUG 16) | Micro dilution | 4.00mg/ml/1.25-25mg/ml | (Al-Fatimi et al. 2005) |
| *G. applanatum* | MeOH | Fruiting bodies | *E. coli* (ATCC 25922) | Micro dilution | ND | (Zengin et al. 2015) |
| *G. lucidum* | EtOH and H$_2$O | Fruiting bodies | *S. aureus* (MTCC 96), *B. cereus* (MTCC 430), *P. aeruginosa* (MTCC 424) | Micro dilution | 80-200mg/ml/ND | (Kansu & Rai 2012) |
| *G. lucidum* | Hexane and chloroform | Fruiting bodies | *S. aureus* (ATCC 6538), *B. subtilis* (ATCC 6633) | Micro dilution | 6.25mg/ml/ND | (Vazirian et al. 2014) |
| *G. lucidum* | Hexane and chloroform | Ergosta-5,7,22-trien-3β-yl acetate (11), ergosta-7,22-dien-3β-yl acetate (70), ergosta-7,22-dien-3-one (15), ergosta-7,22-dien-3β-ol (13), ergosta-5,7,22 trien-3β-ol (12), ganoderadiol (20) | *S. aureus* (ATCC 6538), *B. subtilis* (ATCC 6633) | Micro dilution | 2.5-5mg/ml/ND | (Vazirian et al. 2014) |
| *G. lucidum* | Hot H$_2$O | Carpophores | *B. anthracis* ATCC 6603, *B. cereus* ATCC 27348, *B. subtilis* ATCC 6633, *M. luteus* ATCC 9341, *S. aureus* ATCC 25923, *E. coli* ATCC 25922, *K. oxytoca* ATCC 8724, *K. pneumoniae* ATCC 10031, *P. vulgaris* ATCC 27853, *S. typhimurium* ATCC 6229 | Micro dilution | 1.25-5.0mg/ml/ND | (Yoon et al. 1994) |
| *G. lucidum* | 96% EtOH | Basidiocarps | *B. cereus* (clinical isolate), *M. flavus* ATCC 10240, *S. aureus* ATCC 6538, *L. monocytogenes* NCTC 9793, *E. coli* ATCC 35218, *E. cloacae* (human isolate), *P. aeruginosa* ATCC 27853 and *S. typhimurium* ATCC 13311 | Micro plate Agar, Disc fusion Assay | 1–3.4mg/ml/1.4–4.0mg/ml | (Člerdzic et al. 2014) |

(Continued)
Mycelia (Protein extract) 95% EtOH 12β-acetoxy-3β-hydroxy-7α-β-dihydroxy-acetoxy-7α-hydroxy-15α,22-triacetoxy-8,24-dien-26-oic acid butyl ester, (24R, 22S, 24 R)-7α-hydroxy-3β-β,15α,22-triacetoxy-8,24-dien-26-oic acid, (24R, 22S, 24 R)-3β-β,15α,22-triacetoxy-7α-hydroxy-8,24-dien-26-oic acid.

**S. aureus, S. epidermidis, B. subtilis, B. cereus, E. coli, P. aeruginosa**

**M. tuberculosis**

Micro dilution 68.5 µg/mL/0.035 ml/0.0125 ml/0.035 ml/1.5 mg/ml/20 µg/ml ND.

**P. aeruginosa**

Micro dilution 0.0125 µg/ml/0.035 µg/ml/0.75 mg/ml/0.781-50 µg/mL/ND.

**0.75 µg/ml/0.035 µg/ml**

**0.75 mg/ml/0.035 µg/ml/0.781-50 µg/mL/ND**

**0.75 mg/ml/0.035 µg/ml/0.781-50 µg/mL/ND**

**81.5-512 mg/ml/ND**

**NG**

**G. lucidum**

**Colossolactone A** from G. lucidum was isolated from the chloroform extract of G. lucidum with an IC₅₀ value of 15.2 mM, 12.4 mM and 18.1 mM, respectively (Wang & Ng 2006).

Triterpenoids like applanoxic acids A (1), C (2) and F (3) isolated from G. annulare inhibit the growth of the fungi Microsporum cannis and Trichophyton mentagrophytes at concentrations of 500–1000 µg/ml (Smania et al. 2003).

In another study, researchers synthesised the complexes of polysaccharide with different rare earth metal (RE–CGAP (RE: La, Eu and Yb)) and evaluated their efficacy against fungi and reported that rare earth carboxymethylated G. Applanatum polysaccharide (RE–CGAP complexes with antifungal activities with EC₅₀ value of 1.01–28.48 mg/ml (>100 mg/ml not included) (Sun et al. 2014). The details of the antifungal action of Ganoderma sp. are demonstrated in Table 2.

### 6. Antiviral activities of compounds and extracts from Ganoderma sp

It is interesting to note that the majority of antiviral investigations on Ganoderma sp. have been performed from fruiting body against the protease enzyme of HIV virus. The compounds ganoderiol F (22) and ganodermanontriol (23) were found to be active as anti-HIV-1 agents with an inhibitory concentration of 7.8 µg/ml. In addition, in the same experiment ganoderiol B (51), ganoderiol A (21), ganoderic acid A (76), ganoderic acid B (77), ganoderic acid C1 (78) and ganoderic acid H (79) were found to be moderate in their efficacy (El-Mekkawy et al. 1998; El Dine et al. 2008). Colossolactone types of triterpenoids such as colossolactone V (10), colossolactone VII (8), colossolactone VIII (7), schisanlactone A (33), carboxymethylated polysaccharide (RE–CGAP) and ganomycin B (28) were isolated from the chloroform extract from G. lucidum with and IC₅₀ value of 5–39 µg/ml (El Dine et al. 2008). Similarly in Sato et al. (2009), isolated lanostane-type triterpenoids-ganoderiol F (22), ganoderic acid GS-2 (48) and 20-hydroxyxidicenic acid N (74), 20(21)-dehydroxylidicenic acid N (39) from CHCl₃ extract of the fruiting body of G. sinense and demonstrated the anti-HIV-1 protease activity with IC₅₀ values of 20–40 µM (El Dine et al. 2008; Sato et al. 2009). Compounds from the CHCl₃ extract of the fruiting bodies of G. colossum, farnesyl hydroquinone, ganomycin I (29) and ganomycin B (28), competitively inhibit the active site of HIV-1 protease enzyme with IC₅₀

### Table 2

| Tested bacteria strains | Tested extracts | Reference |
|------------------------|----------------|-----------|
| S. aureus | Mycelial extract | Liu et al. 2014 |
| S. epidermidis | Mycelial protein extract | Liu et al. 2014 |
| B. subtilis | Mycelial extract | Liu et al. 2014 |
| B. cereus | Mycelial extract | Liu et al. 2014 |
| E. coli | Mycelial extract | Liu et al. 2014 |
| P. aeruginosa | Mycelial extract | Liu et al. 2014 |
| M. tuberculosis | Mycelial extract | Liu et al. 2014 |
values of 7.5 and 1.0 μg/ml, respectively (El Dine et al. 2008).

*Ganoderma pfeifferi* triterpenes, ganoderadiol (20), lucidadiol (30) and apllanoxidic acid G (4), were active against influenza virus type A with EC₅₀ of greater than 0.22 mM, 0.22 mM and 0.19 mM, respectively (MothanaRa et al. 2003). Similarly other triterpenes such as ganoderone C (26) (IC₅₀: 2.6 μg/ml), lucialdehydye B (31) (IC₅₀:3.0 μg/ml) and ergosta-7, 22-dien-3β-ol (14) (IC₅₀: 0.78 μg/ml) inhibited the growth of Madin-Darby canine kidney (MDCK) cells infected with influenza virus (Niedermeyer et al. 2005). Herpes simplex virus were inhibited by triterpenes such as compound (20) (ED₅₀: 0.068 mM), ganoderone A (25) (IC₅₀:0.075 μg/ml), (31) (IC₅₀:0.03 μg/ml) and compound 14 (IC₅₀: 0.03 μg/ml), whereas compounds 21 and 51 were less effective in comparison (MothanaRa et al. 2003; Niedermeyer et al. 2005). *G. lucidium* triterpenes lanosta-7, 9 (11), 24-trien-3-one, 15; 26-dihydroxy (GLTA) (40) and ganoderic acid Y (19) possess inhibitory action towards enterovirus 71 with IC₅₀ value of 0.16–4 μg/ml (Zhang et al. 2015). The details of the antiviral activities of *Ganoderma* sp. have been illustrated in Table 3.

7. Anti-parasitic activities of compounds and extracts from *Ganoderma* sp

Nortriterpenes-ganoboninketals A-C (15–17) obtained from the biochemical analysis of the fruiting bodies of

### Table 2. Illustration of antifungal activities of *Ganoderma* sp. parts, products and compounds.

| Ganoderma Sp. | Extraction Solvent | Parts/products/ compounds | Tested Fungal strains | Method | Antifungal Concentration/ZOI/MIC/MFC/EC₅₀ value | References |
|---------------|--------------------|---------------------------|-----------------------|--------|-----------------------------------------------|------------|
| *G. colossus* | MeOH               | Fruiting bodies           | C. maltosa            | Agar Diffusion Assay | 8mm/2mg/disc-ZOI | (Al-Fattimi et al. 2005) |
| *G. applanatum* | MeOH& H₂O         | NG                        | A. clavatus and C. parasilosis | Broth Micro dilution | 1.25 & 2.5mg/ml-Antifungal activity 1.25 & 2.5mg/ml-Antifungal activity | (Zengin et al. 2015) |
| *G. resinaceum* | MeOH& H₂O         | NG                        | A. clavatus and C. parasilosis | Broth Micro dilution | 0.5-308mg/ml-MIC; 1.0–4.0mg/ml-MFC | (Cideržić et al. 2014) |
| *G. lucidium* | 96%EtOH            | Fruiting bodies           | Acremonium strictumBEOFB10m, A. flavusBEOFB21m, A. fumigatusBEOFB22m, A. nigerBEOFB23m, A. nidulansBEOFB24m, A. terreusBEOFB26m, T. virideBEOFB61m | Disc-diffusion & Micro dilution | 0.005–15mg/ml-MIC; 0.1–4.5mg/ml-MFC | (Heleno et al. 2013) |
| *G. lucidium* | MeOH               | Fruiting bodies           | A. fumigatus(human isolate), A. versicolor(ATTCC 11730), A. zochraceus(ATTCC 12066), A. niger (ATTCC 6275), T. viride IAMs0561, P. funiculosum(ATTCC 36839), P. ochrochloron(ATTCC 9112)and P. verrucosum var. cyclopium (food isolate) | Micro dilution | 0–568.30mg/ml-MIC | (Sun et al. 2014) |
| *G. lucidum* | EtOH& chemical synthesis | RE–CGAP(RE: La, EuandYb) | V. mali, F. oxysporum, G. graminis, C. gloeosporioides, A. brassicae | Disc diffusion | 1.85–568.30mg/ml-MIC | (Wang & Ng 2006) |
| *G. lucidum* | dH₂O         | Ganodermin Botrytis cinerea, F. oxysporum and Physalo sporapiricola | M. canis & T. mentagrophytes | Paper Disks | 8.1–12.4M-MF Anti fungal | (Smania et al. 2003) |
| *G. annulare* | NG              | Applanoxidic acids A(1), C(2) & F(3) | M. canis & T. mentagrophytes | Micro dilution | 500 to 1000mg/MF Anti fungal | (Cideržić et al. 2016) |
| *G. applanatum* | 96%EtOH            | Mycelia Acremonium strictum, A. glaucus, A. flavus, A. fumigatus, A. niger, A. terreus, T. viride | Micro dilution | 1.00–2.00mg/ml-MIC; 1.17–4.00mg/ml-MFC | (Cideržić et al. 2016) |
| *G. cinnamomeum* | 96%EtOH            | Mycelia Acremonium strictum, A. glaucus, A. flavus, A. fumigatus, A. niger, A. terreus, T. viride | Colorimetric | 0.83–2.00mg/ml-MIC; 2.00–3.33mg/ml-MFC | (Cideržić et al. 2016) |
| *G. lucidum* | 96%EtOH            | Mycelia Acremonium strictum, A. glaucus, A. flavus, A. fumigatus, A. niger, A. terreus, T. viride | Colorimetric | 0.50–2.00mg/ml-MIC; 1.17–4.00mg/ml-MFC | (Cideržić et al. 2016) |

MeOH: Methanol; EtOH: Ethanol; dH₂O: Distilled water; NG: Data Not Given; ZOI: Zone Of Inhibition; MIC: Minimum Inhibitory Concentration; MFC: Minimum Fungicidal Concentration; EC₅₀: Concentration; RE–CGAP: Rare Earth-CarboxymethylatedGanodermaapplanatum Polysaccharide; μM: Micro Mole; mg/ml: milligram/millilitre.
**Table 3. Illustration of antiviral activities of *Ganoderma* sp. parts, products and compounds.**

| *Ganoderma* sp. | Tested Viral strains | Extraction Solvent | Parts/products/compounds | Method | IC<sub>50</sub> (≤<sup>50μM)/EC<sub>50</sub>/ED<sub>50</sub> value | References |
|-----------------|----------------------|-------------------|--------------------------|--------|-----------------------------|------------|
| G. sinense      | HIV 1 (HIV-1 protease) | CHCl<sub>3</sub> | Ganoderonic acid GS-2(48), 20-hydroxylucidenic acid N(74), 20(21)-dehydrolycidenic acid N(39) & ganoderol F(22) | In vitro (Enzymatic) | 20 – 40μM | (Sato et al. 2009) |
| G. colossum     | HIV 1 (HIV-1 protease) | CHCl<sub>3</sub> | Colossolactone VII(10), Colossolactone VII(8), Colossolactone VIII(7), Schisanlactone A(33), Colossolactone G(5), Colossolactone A(9) | In vitro (Enzymatic) | 5-39μg/mL | (El Dine et al. 2008) |
| G. colossum     | HIV 1 (HIV-1 protease) | CHCl<sub>3</sub> | Ganomycin I(29) & Ganomycin B(28) | In vitro (Enzymatic) | 7.5 and 1.0 μg/mL | (El Dine et al. 2009) |
| G. lucidum      | HIV 1 (HIV-1 protease) | MeOH | Ganoderol F(21) & Ganodermanontriol(23) | In vitro (Enzymatic) | 7.8μg/mL | (El-Mekawy et al. 1998) |
| G. lucidum      | Herpes Simplex Virus types 1 (HSV-1) and 2 (HSV-2), Influenza A virus (Flu A) and Vesicular Stomatitis Virus (VSV) Indiana and New Jersey strains | H<sub>2</sub>O & MeOH | Carpophores | Cytopathic Effect (CPE) Inhibition Assay & Plaque Reduction Assay | 68-1790μg/mL-EC50 | (Eo et al. 2000) |
| G. lucidum      | HSV-1 and HSV-2 | H<sub>2</sub>O/MeOH | Acidic protein bound polysaccharide | Plaque Reduction Assay | | (Eo et al. 2000) |
| G. lucidum      | Oral Human Papillomavirus (HPV) | NG | Fruiting bodies | In vivo (Human) | 87% clearance of virus | (Donatini 2014) |
| G. lucidum      | Newcastle Disease Virus (anti-neuraminidase) | MeOH, EtOAc & Butanol | | In vitro | Virus dilution ratio: 1:16, 1:32 | (Shamaki et al. 2014) |
| G. lucidum      | Epstein-Barr Virus | MeOH | Fruiting bodies | In vitro | 96–100% at 1 103 mol ratio/TPA | (Watatsuki et al. 2003) |
| G. lucidum      | Hepatitis B virus | NG | mycelia | In vitro (HepG2 cells) | IRA(HBsAg, HBeAg) up to 100% Inhibition of production of HBV surface antigen and HBVe at 8μg/ml | (Y. Li et al. 2006) |
| G. lucidum      | Hepatitis B | H<sub>2</sub>O and CHCl<sub>3</sub> | mycelia(Ganoderic acid) | In vitro (HepG2215) | | (Y.-Q. Li & Wang 2006) |
| G. pfeiffer     | Influenza virus type A and HSV type 1 | NG | Ganodermadiol(20), lucidadiol (30) & applanoxic acid G(4) | Dye Uptake Assay | Influenza ED50(0.19–0.22mmol/l); HSV 1 (0.068 mmol/l for ganodermadiol) | (Mothenar et al. 2003) |
| G. pfeiffer     | HSV type 1 | CH<sub>2</sub>C<sub>2</sub> | Ganoderone A(25), Lucialdehyde B(31), Ergosta-7,22-dien-3-ol(14), Ganaderol A(21) & Ganoderol B(51) | In vitro (Vero cells) | 0.03–0.75μg/ml(IC50) | (Niedermeyer et al. 2005) |
| G. pfeiffer     | Influenza virus type A | CH<sub>2</sub>C<sub>2</sub> | Ganoderone C(26), Lucialdehyde B(31) & Ergosta-7,22-dien-3-ol(14) | In vitro (MDCK cells) | 0.78–2.6μg/ml(IC50) | (Niedermeyer et al. 2005) |
| G. lucidum      | Enterovirus 71 | NG | Lanosta-7,9(11),24-trien-3-one,15,26-dihydroxy (GLTA)(40), Ganoderic acid Y(19) | In vitro (Human | Rhabdomyosarcoma) | 0.16 to 4 μg/ml(IC50) | (W. Zhang et al. 2014) |

MeOH: Methanol; EtOH: Ethanol; H<sub>2</sub>O: water; NG: Data Not Given; IC<sub>50</sub>: half-maximal Inhibitory Concentration; EC<sub>50</sub>: half-maximal Effective Concentration; ED<sub>50</sub>: median effective dose; μM: Micro Mole; mg/m: Milligram/Millilitre; μg/ml: Microgram/millilitre; *(Lucidenic acid P(58), Methyl lucidenate P(59), Methyl lucidenate Q(60), Lucidenic acid A(61), Methyl lucidenate A(62), Lucidenic acid C(63), Lucidenic acid D(64), Methyl lucidenate D2(65), Lucidenic acid E2(66), Methyl lucidenate E2(67), Methyl lucidenate F(68), Methyl lucidenate L(69), Ganoderolic acid E(54), Ganoderic acid F(57), Methyl ganoderate F(56), Ganoderic acid T-Q(54)).
Table 4. Details of anti-parasitic activities of *Ganoderma* sp. parts and compounds.

| Ganoderma sp. | Extraction Solvent | Parts/compounds | Test Parasite | Method | LD<sub>50</sub>/IC<sub>50</sub> value | References |
|---------------|-------------------|-----------------|---------------|--------|-------------------------------|------------|
| *Ganoderma* sp. | EtOAc&MeOH | Fruiting bodies(schisanlactone B(32), Ganodermalactone F(24), colossolactone E(6)) | *P. falciparum* | Micro culture Radioisotope Technique | 6.0–10.0 μM | (Lakornwong et al. 2014) |
| *G. lucidum* | EtOAc&MeOH | Fruiting bodies* | *P. falciparum* | Micro culture Radioisotope Technique | 6.0-20μM | (Adams et al. 2010) |
| *G. boninense* | EtOH | Ganoboninketals A(75) Ganoboninketals B-C(16–17) | *P. falciparum* | DNA Fluorescence Signal Test | 4.0, 7.9, and 1.7 μM | (Ma et al. 2014) |
| *G. lucidum* | EtOH | Crude extract | *P. berghei* | In Vivo Malarial activity | >10 mg/ml | (Oluba et al. 2012) |
| *G. lucidum* | NG | Lectin | *H. glycines* | Parasite Mortality Test | (>10 mg/ml/2hrs, 4.5 mg/ml/24hrs, 1.7 mg/ml/48hrs) | (Zhao et al. 2009) |
| *G. lucidum* | NG | Lectin | *D. dipsaci* | Parasite Mortality Test | >10 mg/ml | (Zhao et al. 2009) |

EtoAc: Ethyl Acetate; EtOH: ethanol; MeOH: Methanol; *P. falciparum*: Plasmodium falciparum; *H. glycines*: Heteroderaglycines; *D. dipsaci*: Ditylenchus dipsaci; NG: Data Not Given; μM: Micro Mole; mg/ml: milligram/millilitre; *(Ganoderic acid DM(35), Ganoderic Acid TR 1(52), Ganoderic Aldehyde TR(37), 23-Hydroxyganoderic Acid S(36), Ganoderic acid S(18), Ganodermannondiol(37), Ganofuran B(49)).

Figure 3. Flowchart of isolation of antimicrobial and anti-parasitic compounds from *Ganoderma* sp.
G. boninense were found to possess anti-parasitic activity against *P. falciparum* with IC$_{50}$ values of 4.0, 7.9 and 1.7 μM, respectively (Adams et al. 2010; Ma et al. 2014). Similarly three triterpenes – schisanlac-tone B (32), ganodermalactone F (24) and colossolactone E (6) – isolated with EtOAc and MeOH from *Ganoderma* sp. KM01 are active against *P. falciparum* in the range 6.0–10.0 μM (Lakornwong et al. 2014a). In addition, *G. lucidium* terpenes – ganoderic acid DM (35), ganoderic acid TR1 (52), ganoderic aldehyde TR (37), ganoderic acid S (18), ganodermanondiol (38) and ganofuran B (49) – isolated from EtOAc inhibit *P. falciparum* with IC$_{50}$ value of range 6.0–20 μM (Adams et al. 2010). In a recent study, Zhao et al. found lectin to be active against the plant nematodes *Heterodera glycines* and *Ditylenchus dipsaci*, though their potency was not significant to be used practically (Zhao et al. 2009).

8. Conclusion and future perspective

*Ganoderma* sp. has been used for treatment in various diseases over a long period (Paterson 2006). Our review clearly showed that compounds from *Ganoderma* sp., under the extensive in vivo and pharmacological research, can be used in various microorganisms and parasitic diseases. However, the in vivo experiment and pharmacological research of the identified compounds are very limited. Therefore, future work should be focused on in vivo and pharmacological assays of known compounds, especially Ganoderma terpenes that have antimicrobial and anti-parasitic properties. A better understanding of the antimicrobial and anti-parasitic compounds from *Ganoderma* sp. is crucial for identifying the potential side effects and trace out the new host target and molecular mechanisms, which will provide evidence to further clinical applications of these compounds.

Although extensive researches have been carried out on *Ganoderma* sp., most of the studies were concentrated on few species, *G. lucidum* for instance. Researchers must need to pay more attention to closely related species based on the phylogenic analysis though numerous challenges including genetic analysis, biosynthetic metabolism, separation, isolation and identification may be encountered. In addition, due to the rapid emergence of drug resistance in microorganisms and parasites, fewer options have been left for the treatment of diseases caused by microorganism and parasites. To fight back this problem, further research should be focused on this field for all the identified compounds and the unidentified compounds, which are on the way to be identified. Our review revealed numerous extracts of *Ganoderma* sp. exhibit the inhibition to microorganisms including parasites, indicating that *Ganoderma* sp. in particular still seem to possess opportunities for new drug lead compounds.

Scanty literatures are found on the assay of identified compounds for animal and plants pathogens including parasites, indicating that this area of research for the *Ganoderma* sp. compounds is overlooked. Also, our current experience on a literatures review of *Ganoderma* sp. compounds, more than 430 compounds identified (Baby et al. 2015; Rai et al. 2015), most of the compounds have not been performed on the antimicrobial and anti-parasite assay. Therefore, further studies need to be carried out in order to explore this concealed area.

No doubt, it is evident that *Ganoderma* sp. is going to serve as one of the potential sources of novel antibiotics and anti-parasitic drugs in the near future. To reach the apex and specificity of effective antimicrobial and anti-parasite activity, cooperative investigations need to be carried out in the areas of genomic, bioinformatics, chemistry and pharmacology. Moreover, strategies to evoke the sleeping gene clusters linked for the production of bioactive compounds and its regulation need to be adopted.

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