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In-Vitro Antibacterial Activity of some Ganoderma Species: A Review

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Abstract

The rising significance of personal health and wellbeing has spurred scientific interest in natural research on products. Numerous phytochemicals that are found naturally in plants, fruits, and vegetables have been discovered to have biological activity and are frequently hailed as being good for human health. In addition to current treatment approaches, herbal medications may be a safe and effective way to treat infectious infections. *Ganoderma* has long been used for the management of incessant infectious conditions such diabetic foot ulcers, pneumonia, and chronic hepatitis. While there is little information on *Ganoderma's* antiviral and antibacterial properties in humans, preliminary (*in vitro* and *in vivo*) research show that the plant possesses a wide range of these properties. Furthermore, gram-positive and gram-negative bacteria are inhibited *in vitro* by antibacterial components found in *Ganoderma* species. The outcomes of preclinical (*in vitro*) and clinical investigations on the antibacterial and antifungal properties of *Ganoderma* species are brought to light in this review.

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Diabetic Foot Ulcer

Diabetic foot ulcers (DFUs) are a frequent and possibly dangerous diabetic consequence[1]. Out of the 537 million individuals with diabetes globally, 19 to 34% will experience a DFU at some point in their lives[2]. It is an open sore or wound that typically develops on the foot's bottom or toes[3]. It is caused by a number of diabetes-related conditions, some of which are difficult to cure. The main causes of DFU include a combination of neuropathy (nerve damage) and poor blood circulation, peripheral neuropathy (nerve damage), poor circulation, foot deformities (bunions, hammertoes),

calluses or corns, trauma or pressure on the feet, inadequate foot care and Obesity. Reduced blood circulation hinders the body's ability to heal and fight infections and increases the risk of developing diabetic foot ulcers.

Diabetic foot ulcer's symptoms and signs may include an open sore, redness, swelling, warmth, drainage or pus or signs of infection. It can lead to severe complications if left untreated, including cellulitis (skin infection), osteomyelitis (bone infection), gangrene (tissue death) and the potential need for limb amputation. About 20% of individuals with DFU will need lower-extremity amputations, either major (above the ankle), minor (below the ankle), or both. Ten percent of DFU patients will die within a year of their first diagnosis [4]. In some cases, systemic infections can occur, which can be life-threatening.Preventing DFU is a crucial aspect of diabetes care[5]. The healing process of a typical wound progresses through four stages: hemostasis, inflammation, proliferation, and remodelling.However, a diabetes patient's constant hyperglycaemia has an effect on a number of normal wound healing processes [6]. Wound healing in it can be a time-consuming process and the time it takes for complete healing can vary significantly from person to person. It is crucial for individuals with diabetes to seek prompt medical attention for any foot ulcer and to follow the recommendations of their healthcare team to optimize the chances of successful wound healing and prevent complications [7]. This involves maintaining good blood sugar control, regularly examining the feet for any signs of injury or pressure points, wearing comfortable and properly fitting shoes, practising proper foot hygiene, avoiding walking barefoot and seeking professional podiatric care. In more severe cases, surgical intervention may be necessary. DFU requires careful monitoring and management [8][9], often involving a healthcare team that may include podiatrists, wound care specialists and endocrinologists. Preventive care and early detection are crucial in avoiding the development of diabetic foot ulcers and their complications.

Diabetic foot ulcer is a polymicrobial infection harbouring different bacteria. Diabetic foot infections (DFI) are composed of a mixture of Gram positive (*Staphylococcus aureus, Bacillus subtilis, Streptococcus and Enterococcus spp*) and Gram negative (*Escherichia coli, Klebsiella pneumoniae, Morganella morganii, Entrobacter, Pseudomonas, Citrobacter, Salmonella* and *Proteus* sp.) bacteria [10]. Among these multi drug resistance is one of the challenges faced by the therapists.In addition to determining the lesion's origin, the analysis is conducted to determine whether the ulcer is neuropathic, ischemic, or neuro-ischemic and provide details about its size, depth, appearance, and location.

Ganoderma and its species

Ganoderma is one of the most popular and important wild medicinal mushrooms Genus that has been therapeutically used since thousands of years [11]. Numerous studies and research have confirmed the multidirectional biological activity of extracts from various *Ganoderma* spp. and isolated compounds. The following properties have been proven anti-diabetic [12], hypoglycaemia, anti-cancer [13], anti-inflammatory, anti-tumour [14], anti-oxidant [15], immunomodulatory, anti-viral, anti-bacterial [16], anticonvulsant, anti-fungal, antihypertensive, anti-atherosclerotic, anti-aging, anti-androgenic, anti-hepatotoxic, radical scavenging property, neuroprotection, sleep promotion, cholesterol synthesis inhibition, inhibition of lipid peroxidation/oxidative DNA damage, hepatoprotective properties, maintenance of gut health, prevention of obesity and stimulation of probiotics [17].The most important groups of compounds found in *Ganoderma* spp. include triterpenes (*Ganoderma* triterpenes) and polysaccharides. Until now, more than 300 triterpenes and 200 polysaccharides

characterized by diverse chemical structures and biological activity have been isolated.It includes several species of mushrooms, each with its own characteristics and properties. Some of the most well-known *Ganoderma* species include:

Ganoderma applanatum

Also known as the Artist's Conk, this species has a woody appearance and is commonly found in North America and Europe. While it may not be as well-studied as some other Ganoderma species, it is used in traditional medicine for its potential medicinal properties [18]

Ganoderma boninense

G. boninense is a species of *Ganoderma* fungus whichis a close relative of *G. lucidum* and it is native to various regions in Asia and has a more distinctive reddish-brown cap compared to other *Ganoderma* species. It is used in traditional medicine in certain Asian countries and is also under research for its potential health benefits.

Ganoderma lucidum

*G. lucidum*commonly known as Lingzhi or Reishi, and one of the most widely studied and revered species in traditional Chinese medicine. It has a glossy, varnished appearance and is known for its potential immunomodulatory, anti-inflammatory, antidiabetic and antioxidant properties. It is often used in herbal remedies and dietary supplements such as capsules, extracts, teas and dried slices [19].

Ganoderma tsugae (Hemlock Reishi)

This species, often called the Hemlock Reishi, is native to eastern North America and is closely related to*G. lucidum*. It is primarily found growing on hemlock trees (Tsuga species) and shares many of the potential health benefits of its close relative.*G. tsugae* is less common in commercial health products, but it can still be found in various forms such as dietary supplements, extracts and teas.

Ganoderma resinaceum

The Hemlock Varnish Shelf, is another species found in North America and Europe. It has a varnished cap and can grow on hardwood trees and not limited to a specific host tree and can be found on a variety of deciduous and coniferous trees. It is known for its potential medicinal properties, similar to other *Ganoderma* species.

Ganoderma australe

This species is found in Australia and parts of Southeast Asia. It shares some similarities with other*Ganoderma* mushrooms and is also used for its potential health-promoting properties.

These are just a few examples of *Ganoderma* species and there are many more within the genus such as *G. pfeifferi*, *G. oregonense, G. multipileum. G.adspersum, G. sessile, G. lipsiense, G. colossus, G. curtisii, G.lobatum, G. mbrekobenum*, *G. sinense, G. tornatum, G. tuberculosum*, *G. zonatum, G. miniatocinctum* and *G. weberianum* etc.

Hypoglycemic activity is demonstrated by numerous compounds present in the extracts of *G. lucidum*: polysaccharides, proteoglycans, proteins, and triterpenes. It is presumed that *G. lucidum* extracts may be an alternative adjuvant treatment for diabetes. The mechanism of action of polysaccharides is by increasing insulin levels and lowering blood glucose levels.A study on mice with type 2 diabetes showed that *Ganoderma spp*. is effective in regulating blood glucose levels and has a positive effect on the lipid profile; therefore, it is considered a good candidate in the treatment of type 2 diabetes with comorbid metabolic disorders. Ganoderan A and B isolated from an aqueous extract of *G. lucidum* showed anti-glycaemic properties. The Ling-Zhi-8 protein is effective in type 1 diabetes due to its immunomodulatory properties [20]. Ganodermin is a protein with antifungal activity isolated from *G. lucidum*. It inhibits the growth of *Botrytis cinerea, Fusarium oxysporum*, and *Physalosporapiricola.*

Exopolymers of *G. applanatum* noticeably decrease blood glucose levels. Ergosterol peroxide isolated from *G. applanatum* can inhibit aldose reductase, an enzyme which is involved in the development of diabetic complications (neuropathy and retinopathy); therefore, reductase inhibitors may be useful in their prevention. The latest reports have indicated the hypoglycaemic effect of extracts from two other species: *G. pfeifferi* and *G. resinaceum*. The aqueous extract of *G. resinaceum* led to a slight decrease in glycemia in alloxan-induced diabetic rats.

Ethanolic extracts obtained from mycelium *G. applanatum*, *G. carnosum* and *G. lucidum* also demonstrated antifungal activity. They were effective against *Acremonium strictum, Aspergillus glaucus, Aspergillus flavus, Aspergillus fumigatus, Aspergillus nidulans, A. niger, Aspergillus terreus* and *Trichoderma viride.*

Antimicrobial activity

Genus *Ganoderma* has antimicrobial components that stop the growth of fungi, viruses and both gram-positive and gram-negative bacteria are inhibited from growing. Multidrug resistance (MDR) bacterial and fungal infections may be successfully treated with natural antimicrobial substances derived from a wide variety of medicinal plants [21]. *Ganoderma* extracts contain substances with antibacterial properties, which are caused by phytochemicals synthesised in the plant's secondary metabolism [22][23]. According to the World Health Organisation (WHO), medicinal plants would be the best source to obtain a range of medications. Plants include a number of secondary metabolites that have been shown to have antibacterial effects in vitro, including tannins, alkaloids, phenolic compounds and flavonoids [24][25].

Ganoderma species, contain bioactive compounds such as polysaccharides, triterpenes and peptides, with demonstrated antibacterial properties. These compounds exhibit a broad-spectrum antimicrobial activity, making them effective against a range of bacterial strains. Studies have indicated that extracts from *Ganoderma* species can inhibit the growth and multiplication of pathogenic bacteria commonly found in diabetic foot ulcers. This includes both Gram-positive (*Staphylococcus aureus, Enterococcus faecalis, Bacillus subtilis, Enterococcus faecium* and *Streptococcus pneumoniae*

etc) and Gram-negative (*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, salmonella typhimurium*and *Proteus vulgaris* etc*)* bacteria. Bacterial biofilms are often implicated in chronic wound infections, including diabetic foot ulcers. *Ganoderma* extracts have demonstrated the ability to disrupt biofilms formed by pathogenic bacteria, making it easier for the immune system and antimicrobial agents to target and eliminate the bacteria.

There are many different methods are used to extract different bioactive metabolite from*Ganoderma*. Some of the methods which we are discussing here, are being used in today's time:

Numerous extracts obtained from Ganoderma with varying polarity (from non-polar to polar) have been utilised in scientific studies to explore the wide range of metabolites, including polysaccharides, triterpenoids, and phenols [26], alkaloids etc., present within this fungus. These extracts possess distinct chemical profiles, enabling targeted exploration of specific metabolite classes and their associated biological activities [27].

AgNO3 was reduced to produce silver nanoparticles via a green process mediated by mycelial extracts of*G. lucidum* have improved stability and excellent dispersion in an aqueous solution, (AgNPs). Compared to other metal NPs, AgNPs have more antibacterial activity against multidrug-resistant bacteria. Gram-positive and Gram-negative bacterial and yeast strains were used to assess the synthetic nanoparticles' antibacterial efficacy. Because the pathogens were inhibited in their multiplication, the environment and public health were less at danger due to the effectiveness of the silver nanoparticles [28].

Using an environmentally friendly process, copper oxide nanoparticles (CuONPs) were created from the supernatant and extract of the fungus *G. sessile*, and their antibacterial and biocompatibility characteristics were identified.CuONPs showed antimicrobial activity against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa*.Further research might be done on the CuONPs created from the fungus *G. sessile* extract in order to see whether they are effective in treating superficial infectious illnesses. [29].

A green method was used to create new biogenic silver (AgNPs) and gold nanoparticles (AuNPs) using G. lucidum extract. B. subtilis showed the greatest growth suppression activity of GL-AgNPs, followed by B. cereus, P. aeruginosa, E. coli, and S. aureus [30].

Zinc oxide (ZnO) nanoparticles with different concentrations of*G. lucidum* extract have been biologically produced, and their optical, morphological, structural and elemental properties have been identified. The use of green generated ZnO with *G. lucidum* extracts as a nanonutrient is first documented in the study by Sedefoglu*et al.,* 2022 [31].

Novel anti-biofilm strategies must be designed to include natural bio products instead of common antibiotics. Mushrooms are a nutritionally functional foods and a source of pharmaceuticals functions such as antidiabetic, antitumor, immunomodulating, antioxidant, cardiovascular, anti-hypercholesterolemia, antimicrobial. *Ganoderma,* especially *G. lucidum* have a notable activity against biofilms [32].

Table 1.

Species	Bacteria	Remark	Reference
Ganoderma sessile	*Staphylococcus aureus*	CuONPs-S (Copper oxide nanoparticles- *S. aureus*) were more cytotoxicto kidney cells and macrophages, and the hepatocytes	[33][34][35]
	Escherichia coli		
	Pseudomonas aeruginosa	CuONPs-E (Copper oxide nanoparticles-*E. coli*) were less cytotoxic to kidney cells and macrophages, and the hepatocytes	
Ganoderma boninense	*Staphylococcus aureus*	The highest antibacterial activity was observed in chloroform-extracted GBMA (*G. boninense* media agar) against all tested bacteria	[36][37][38]
	Streptococcus pyogenes		
	Pseudomonas aeruginosa	Methanol-extracted GBMA exhibited higher and broader ranges of antibacterial activity against *S. aureus*	
	Klebsiella pneumonia		
	Escherichia coli	Methanol and acetone extracted GBFB (extract of *G. boninense* fruiting bodies) and GBMA demonstrated lower antibacterial activity than chloroform extracted GBMA	
		GBMB (*G. boninense* media broth) did not exhibit any antibacterial activity against *S. aureus*, MRSA, and *K. Pneumonia*	
Ganoderma lucidum	*Acidovorax avenae*	Only the methanol and water extracts showed inhibition of all the phytopathogens tested.	[39][40][41]
	Agrobacterium rhizogenes		
	Agrobacterium tumefaciens		
	Brenneria quercina		
	Burkholderia cepacian		
	Erwinia carotovora	*Erwinia carotovorasubsp. carotovora* and *P. syringae pv. phaseolicola* were the most inhibited, whereas P. syringae pv. syringae was least inhibited	
	Pseudomonas fluorescens	Culture fluids of *G. lucidum*, inhibited both gram-positive and gram-negative plant pathogenic bacteria	
	Pseudomonas syringae pv. Syringae		
	Rathayibacter tritici		
	Xanthomonas campestris pv. Campestris		
Ganoderma lipsiense	*Staphylococcus aureus*	Crude extract of *G. lipsience* and their fractions dichloromethane and ethyl acetate showed antibacterial activities against *Pseudomonas aeruginosa* and *Staphylococcus aureus* at 500 µg mL^{-1}.The production of ergosta-6,22-diene-3β,5α,8α-triol by *G. lipsiense* showed antiparasitic activity against *Giardia duodenalis* throphozoites	[42][43][44]
Ganoderma lipsiense	*Pseudomonas aeruginosa*		
Ganoderma austral ***Ganoderma applanatum*** ***Ganoderma curtisii*** ***Ganoderma lobatum*** ***Ganoderma lucidum*** ***Ganoderma oregonense*** ***Ganoderma resinaceum***	*Escherichia coli*	The nucleotide sequences obtained from all *Ganoderma* strains in this study were deposited in GenBank.	[45]
	Pseudomonas aeruginosa	*G. austral and G. applanatum* extracts showed anti-proliferative activity against the tumor cell at concentration lower than 50 µg/mL	
	Enterococcus faecalis	*G. curtisii* and *G.lucidum* showed anti-proliferative activity and remarkable inhibition values for HeLa cell line	
	Staphylococcus aureus	*G. curtisii* show such growth inhibitory mechanisms in tumor cells	
	Escherichia coli	Triterpenoids, (ganoderic acids) responsible for its antitumor activity.	
	Salmonella typhi		
	Staphylococcus aureus (MRSA)		

Ganoderma lucidum	*(MRSA)* *Streptococcus pyogenes* *Bacillus subtilis* *Enterobacter aerogenes* *Corynebacterium diphtheria* *Pseudomonas aeruginosa*	β-Glucans (polysaccharide) develops protective inflammatory responses that prevent infections by pathogens, including infections by corona viruses. *G. lucidum* can be used in the treatment of COVID -19 infections. *G.lucidum* appears to be promising in preventing the pathogenesis of Alzheimer's disease caused by hypercholesterolemia.	[46][47][48]
Ganoderma mbrekobenum	*Bacillus subtilis* *Bacillus cereus* *Fusarium oxysporum*(fungus)	The higher antibacterial activity produced by methanol extract was against all tested pathogens	[49][50][51]
Ganoderma multiplicatum ***Ganoderma sinense***	*Staphylococcus aureus*	The compounds ganosinensin B and ganosinoside A, present in extracts of both *Ganoderma* species showed strong antibacterial activity against *S. Aureus*	[52][53][54][55]
Ganoderma tsugae	*Staphylococcus aureus* *Bacillus subtilis* *Escherichia coli*	Triterpenoids present in *G. tsugae* extract showed strong antibacterial activity against all tested bacteria	[56][57]
Ganoderma tornatum ***Ganoderma tuberculosum***	*Clavibacter michiganensis*	*G.tuberculosum* and *G.martinicense* had the best antioxidant and antibacterial activity	[58][59][60]
Ganoderma lucidum	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa* *Salmonella enteric* *Candida albicans*	AgNPs (silver nanoparticles) were successfully synthesized from *G. lucidum* crude extracts and these colloidal AgNPs demonstrated an extraordinary antimicrobial activity against all tested pathogens	[61][62]
Ganoderma lucidum	*Enterococcus faecalis* *Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa* *B. subtilis*	Methanolic extract of GL exhibited higher antibacterial activity against *E. coli* and *P. aeruginosa* Aqueous extract of GL exhibited higher antibacterial activity against *B. subtilis* and *S. aureus*	[63][64][65][66]
Ganoderma oerstedii, ***Ganoderma weberianum*** ***Ganoderma subincrustatum***	*Staphylococcus aureus* *Escherichia coli*	Antibacterial activity was weak against *S. aureus* All tested *Ganoderma* mushrooms have medicinal potential such as anti-inflammatory and anti-proliferative.	[67][68][69][70]
Ganoderma neojaponicum ***Ganoderma lucidum***	*Salmonella typhimurium* *Salmonella Enteritidis* *Escherichia coli*	compared to *G. lucidum*, *G. neo-japonicum* showed remarkable antibacterial and antioxidant properties	[71][72]

Ganoderma applanatum	*Escherichia coli*	The synthesized AgNPs from methanolic extract of *G. applanatum* exhibit high antioxidant capacity, in vitro antibacterial activity against *S.aureus* and *E. coli and* invivoantifungal activity *G. applanatum* can be efficiently used in synthesis of AgNPs with potent antimicrobial properties, which can be used for both clinical and agrochemical purposes.	[73]
	Staphylococcus aureus		
	Fungus- *Botrytis cinerea*		
	Colletotrichum gloeosporioides		
Ganoderma atrum	*Escherichia coli*	*G. atrum* is a popular remedy to treat conditions such as chronic hepatitis, hypertension,cancer, hyperlipemia, bronchitis, atherosclerosisand diabetes The antibacterial activity of each group was shown as *G. atrum* sterolcomponents> ergosterol>ergosterol ester.	[74][75][76]
	Salmonella enteric		
	Staphylococcus aureus		
	Shigella sonnei		
	Listeria monocytogenes		
Ganoderma applanatum ***Ganoderma lucidum***	*Pseudomonas fluorescens*	Water and methanol extracts of both *Ganoderma* exhibited strong antibiotic activity against all bacterial strains tested.	[77][78]
	Bacillus subtilis		
	Staphylococcus epidermidis		
	Micrococcus luteus		
	Pseudomonas aeruginosa		
Ganoderma lucidum	*Lepidium sativum* (garden cress)	first report of green synthesized ZnO with *G. lucidum* extracts The effect of extract concentration on various properties of ZnO Nano Particles Nano nutrient effect of ZnO NPs on *Lepidium sativum*	[79][80][81]
Ganoderma applanatum, ***Ganoderma lucidum*** ***Ganoderma pfeifferi*** ***Ganoderma resinaceum***	*Pseudomonas aeruginosa*	Chloroform extract of *G. resinaceum* expressed the most potent antibacterial activity against *P. aeruginosa* Aqueous extract of *G. pfeifferi* expressed the most potent antibacterial activity against both *E. coli* and *S. aureus* Ethanol extracts of *G. pfeifferi* and *G. resinaceum* were the most effective against *A. Niger*	[82][83][84]
	Staphylococcus aureus		
	Escherichia coli		
	Aspergillus niger		
Ganoderma boninense	*Staphylococcus aureus* (MRSA)	*G.boninense* extract induces irreversible damage to the cell membrane of MRSA, thus causing cellular lysis and death	[85][86][87]
Ganoderma multipileum	*Klebsiella pneumoniae*	The ZnO nanoparticles synthesized from *G. multipileum* showed a strong antibacterial effect against gram-positive (*K. pneumonia* and *S. aureus*) and gram-negative (*E. Coli* and *P. aeruginosa*) bacteria The ZnO nanoparticles also showed a high antifungal effect against all different fungus	[88][89][90]
	Staphylococcus aureus		
	Escherichia coli		
	Pseudomonas aeruginosa		
	Fungus- *Aspergillusflavus*		

	Aspergillusniger		
	Aspergillus fumigatus		
	Fusarium solani		
	Mucor species		
Ganoderma cochlear	*Staphylococcus aureus*	exhibit potent inhibitory activity against *S. Aureus*	[91][92][93]
Ganoderma pfeifferi	*Staphylococcus aureus*	Extracts of the fruiting bodies of the mushroom exhibited antibacterial activity against all tested bacteria	[94][95][96]
	Bacillus subtilis		
	Escherichia coli		
Ganoderma australe	*Escherichia coli*	The extracts of *G. curtisii*inhibited the growth of *S. aureus* Ganoderic acids, phenolic compounds may also be responsible for antibacterial inhibition and antioxidant activity of all tested *Ganoderma* species	[97][98]
Ganoderma applanatum	*Staphylococcus aureus*		
Ganoderma colossus	*Pseudomonas aeruginosa*		
Ganoderma curtisii	*Enterococcus faecalis*		
Ganoderma lobatum			
Ganoderma oregonense			
Ganoderma resinaceum			
Ganoderma sessile	*Escherichia coli*	A very low concentration of silver nanoparticles produced from the extract of*G. sessile* is required for the bacterial inhibition	[99][100][101]
	Staphylococcus aureus		
	Pseudomonas aeruginosa		

Antimicrobial Activity of *Ganoderma* Species against Gram Positive Bacteria

Fungi are particularly appealing for nano particle synthesis because they release huge amounts of enzymes and metabolites and are facile to manage in the laboratory. Copper and copper oxide NP synthesis has recently attracted attention, as recent research demonstrated that they are advantageous for biomedical applications due to their antibacterial, anticancer, antidiabetic and antioxidant characteristics [61]. Micro, quasi-spherical nanoparticles (NPs) with atypical size of 4.5 ± 1.9 nm and 5.2 ± 2.1 nm were obtained from the resulting supernatant and extract of the fungi *Ganoderma sessile*. CuONPs displayed antibacterial efficacy against *Staphylococcus aureus* (*S. aureus*). The half-maximal inhibitory concentration (IC50) value for *S. aureus*, was 10.2 µg/mL. When bacteria were subjected to CuONPs, their ultrastructural examination confirmed that tiny CuONPs were present throughout the bacterial cells [33]. The mycelial extract of *Ganoderma boninense* was found to be effective in producing secondary metabolites with antibacterial efficacy against *S.aureus* and *S. pyogenes.* Methanol-extracted GBMA exhibited higher and broader ranges of antibacterial activity against *S. aureus* [34]. Additionally, the minimum inhibitory concentration (MIC) of*Ganoderma sinense* and *Ganoderma multiplicatum* extracts demonstrated bactericidal activity against *S. aureus* [52]. Gram-positive and gram-negative plant pathogenic bacteria were suppressed by *G. lucidum* culture fluids. *Rathayibacter tritici* which is a plant pathogen of wheat was inhibited by extracts of *G.luicdum* [39]. The biochemical function of the distillates derived from the in vitro culture of Mexican strains of *Ganoderma* viz. *Ganoderma australe, Ganoderma applanatum, Ganoderma colossus, Ganoderma*

curtisii, Ganoderma lobatum, Ganoderma lucidum, Ganoderma oregonense and Ganoderma resinaceum. The growth of gram-positive *S. aureus* was suppressed by extracts of three strains of*G. curtisii* that exhibited anti-proliferative activity [45]. Research on *G. lucidum* extracts was evaluated on gram-positive and methicillin-resistant bacteria, including *Streptococcus pyogenes*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (MRSA). *Streptococcus pyogenes* ($p = 0.05$) and *Staphylococcus aureus* (MRSA) ($p = 0.022$) were significantly inhibited by hexane extract of*Ganoderma lucidum*. *Streptococcus pyogenes* was the most sensitive microorganism[46]. There are scanty researches on the physiological functions of *G. mbrekobenum's* fruiting bodies. Methanol extract of *G. mbrekobenum* demonstrated greater antibacterial activity against *Bacillus cereus* and *Bacillus subtilis*, measuring 14.13 ± 0.12 mm and 13.03 ± 0.12 mm, respectively. The majority of the test bacterial strains were resistant to the antibacterial effect of the aqueous extracts [49]. The antibacterial activity of *Ganoderma* strains viz. *G. tuberculosum*, *G. tornatum* and *G. weberianum* against *Clavibacter michiganensis*, which causes tomato canker, is highlighted within the concentration range 31.5 to 1000 µg/mL is noteworthy [58]. Bacallao-Escudero et al. (2023) investigated the antibacterial activity of ethanolic extracts of*Ganoderma oerstedii*, *G. weberianum* and *G. subincrustatum* fruiting bodies against *Staphylococcus aureus* and *Escherichia coli* using the broth microdilution method. There was minimal antibacterial activity (MIC50 > 10 mg/mL) against *S. aureus* [67]. The strongest antibacterial activities against the studied pathogens were demonstrated by the "green synthesis" of silver nanoparticles (AgNPs) from *Ganoderma applanatum*. High antioxidant capacity, in vitro antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*, and in vivo antifungal capabilities against*Colletotrichum gloeosporioides* and *Botrytis cinerea* are all displayed by the synthesised Ag nano particles[73]. ZnO nanoparticles synthesised from *Ganoderma multipileum* displayed significant antibacterial activity against gram-positive bacteria, including *Staphylococcus aureus* and *Klebsilla pneumonia* [88]. *G. boninense* is identified as an oil palm pathogen, although there is scanty information about its biological activity. In broth microdilution experiments, high susceptibility was reported in methicillin-resistant *Staphylococcus aureus* (MRSA) in the elute fraction, with a MIC value of 0.078 mg mL1. According to the findings, *G. boninense* extract causes irreversible damage to MRSA cell membranes, resulting in cellular lysis and death [85].

Antimicrobial Activity of *Ganoderma* Species against Gram Negative Bacteria

Gram-negative bacilli are the most common bacterial pathogens and are often resistant to medicinal products. Monitoring for antimicrobial resistance in this population is critical since resistance has been linked to increased morbidity and mortality. CuONPs extracted from the fungi *Ganoderma sessile* displayed antibacterial efficacy against gram-negative bacteria like *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Escherichia coli* (*E. coli*). The half-maximal inhibitory concentration (IC50) values were 4.1µg/mL and 8.5µg/mL, respectively [33]. The mycelial extract of *G. boninense* was found to be effective in producing secondary metabolites with antibacterial activity against *E. coli* and *P. aeruginosa* and *K. pneumonia* [36]. It was observed via liquid-liquid extractions (LLE) that mycelia extraction using a 1:1:1 combination of chloroform, methanol, and water was better at detecting antibacterial activity with the highest concentrations of antibacterial substances. Research have been conducted to isolate and distinguish the antibacterial activity of *Ganoderma lucidum* culture fluids against several gram-negative plant pathogenic bacteria like*Acidovorax avenae, Agrobacterium*

rhizogenes, Agrobacterium tumefaciens, Brenneria quercina, Burkholderia cepacian, Erwinia carotovora, Pseudomonas fluorescens, Xanthomonas campestris. Nearly all of the studied bacteria were unable to grow in the freshly obtained culture fluids of *Ganoderma lucidum. Erwinia carotovora subsp. carotovora* and *P. syringae pv. phaseolicola* were the most inhibited bacteria against the extracts of *G.lucidum. Pseudomonas fluorescens* and *Burkholderia cepacia* did not exhibit any form of activity. There was a little inhibition seen with *Brenneria quercina* [39]. The remarkable antibacterial and anticancer activities of Ganoderma lucidum methanolic extract (GLME) have garnered significant interest. Screening the extract's antibacterial properties against four strains of both Gram-positive and Gram-negative bacteria revealed that it had more antibacterial properties against *E. coli* bacteria than streptomycin, resulting in a zone of inhibition measuring 44 ± 0.09 mm [66]. Furthurmore, colloidal AgNPs derived from *G.lucidum* displayed exceptional antibacterial efficacy against gram negative *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica* and *Candida albicans* in biological assays, with IC50 values of 17.06, 1.32, 54.69 and 27.78 g/mL, respectively [61]. Crude extracts of *G. lipiense*, along with their dichloromethane (DCMf) and ethyl acetate (EAf) derivatives, demonstrated antibacterial activity at 500 µg mL−1 against *Pseudomonas aeruginosa* and *Staphylococcus aureus* [42]. El-Dein et. Al. (2023) demonstrated that the methanolic extract of *G. mbrekobenum* exhibited the strongest antifungal activity against *F. oxysporum* and *F. oxysporum f. sp. Lycopersici* [49]. Experiments comparing the bioactivities of various Ganoderma species have been carried out.*G. lucidum* (GL) and *G. neo-japonicum* (GnJ) were extracted using hot water and their antimicrobial properties were contrasted. The pathogens *Salmonella typhimurium*, *Salmonella Enteritidis* and *Escherichia coli* had minimum inhibitory concentrations (MICs) of 1.25 mg/mL to 2.5 mg/mL for GL and 2.5 mg/mL to 5 mg/mL for GnJ. SEM demonstrated that the two extracts worked by lysing the cells and shrinking the pathogens' cell walls [71]. Investigations were conducted to evaluate the antimicrobial potential of the autochthonous *Ganoderma* species (*G. resinaceum*, *G. pfeifferi*, *G. lucidum* and *G. applanatum*). CHCl3 extract of *G. resinaceum* had the strongest antibacterial activity against *P. aeruginosa*, EtOH extracts of *G. pfeifferi* and *G. resinaceum* were shown to have the strongest antibacterial activity against *A. niger*, whereas *G. pfeifferi* exhibited the maximum antibacterial activity against both *E. coli* and *S. aureus* [82]. ZnO nanoparticles that were isolated from *Ganoderma multipileum* had substantial antibacterial activity against gram-negative bacteria, such as *Eschericia coli* and *Pseudomonas aeruginosa* [88]. AgNPs were produced using *Ganoderma sessile* extracts and supernatants and their *in vitro* antibacterial efficacy against *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* was assessed. Once the minimum inhibitory concentration (MIC) was established, the AgNPs demonstrated antibacterial activity against all employed bacteria. The MIC ranged from 1.26 to 5.0 µg/mL, contingent upon the type of bacterium [99].

Conclusion

Ganoderma species are also known for their wound healing properties. By accelerating the wound healing process, they can indirectly contribute to reducing the risk of infection in diabetic foot ulcers and other wounds. *Ganoderma* species have immunomodulatory effects that can enhance the body's immune response. This can help the immune system combat bacterial infections more effectively, especially in individuals with diabetes, who may have compromised immune function. Inflammation is a key component of the body's response to bacterial infections. *Ganoderma*'s anti-inflammatory

properties can help reduce inflammation associated with diabetic foot ulcers and the corresponding infections.

This potential antimicrobial benefits of *Ganoderma* species for wound care in diabetic foot ulcers can be considered as complementary to standard medical treatment. Consulting with a healthcare professional is essential when using natural remedies like *Ganoderma,* as part of a comprehensive wound care plan. Furthermore, the quality and source of *Ganoderma* products can significantly impact their efficacy, so using reputable products is crucial.

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