VOLUME - 11, ISSUE - 05, MAY - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Microbiology

MEDICINAL PROPERTIES AND ECONOMIC IMPORTANCE OF AgNP FROM *Ganoderma Lucidum*: A REVIEW

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ABSTRACT The medicinal importance of fungi should not be ignored as it plays an important role in fields like Ayurvedic dravyaguna and pharmacognosy. Ganoderma lucidum was reported with rich medicinal properties due to having good number of medicinal compounds. Ganoderma lucidum, an oriental medicinal fungus showing a variety of biological activities like anticancer activity, anti-diabetic activity, hypoglycemic effect, antimicrobial and antioxidant properties. Candida, Enterococcus, Staphylococcus spp, Streptococcus spp, Escherichia, Pseudomonas are leading pathogens present on ear, nose and throat region. In the present decades, there is a much gaining attention to scientists in green synthesis of silver nanoparticles. The present paper provides information about the Medicinal properties and Economic importance AgNP from Ganoderma lucidum.

KEYWORDS : Ganoderma lucidum, AgNP, Medicinal importance,

INTRODUCTION

Several fungi like mushrooms are using as medicine as tradition is important in both in India and western countries (Vaidya and Rabba, 1993). Several antimicrobial compounds like lectins, terpenes, polysaccharides have great potential interest on nutritional and medicinal status of different mushrooms. Most of the fungi are saprophytic and non-pathogenic to several living systems like animals, plants, and other microbial species (De Lucca, 2007). The plant-fungi interactions are mediated by primary and secondary metabolites that are available in environment and have several inferences for medicine (Scherlach et al., 2013).

Fungi are important in both ancient and modern biological processes include brewing, baking, production of organic acids, antibiotics, enzymes, alcohols, and several pharmaceutical products (Bennett, 1998). Symbiotic associations during co-evolution events between plants and fungi results in nutrient exchange and protective mechanisms based on climatic changes based on evolutionary developmental perspective.

Mushrooms that are belongs to fungi are consumed by ancient and **modern** Homo sapiens throughout the world from past to present. Mushrooms like Button mushroom (*Agaricus bisporus)*, Shiitake mushrooms(*Lentinula edodes*),, Oyster mushrooms (*Pleurotus ostreatus)*, Shimeji mushroom (*Hypsizygus tesselatus*), Porcini mushrooms (Boletus edulis) and Paddy straw mushroom (*Volvariella volvacea)* are rich with guanylic acid, glutamic acid, aspartic acid, protein, fibre, iron, vitamin B, vitamin C, vitamin D, beta-glucan, folic acid, potassium and copper. These can control diseases like diabetics, cancer and weak bones. The mushrooms has numerous health benefits such as better immune function, lowers bad cholesterol, boosts heart health, absorption of calcium, improved metabolic processes and maintain strong bones.

FUNGI IN MEDICINAL IMPORTANCE

The medicinal importance of fungi should not be ignored as it plays an important role in fields like Ayurvedic dravyaguna and pharmacognosy (Vaidya and Rabba, 1993). Members of fungal genera Inonotus and Phellinus are well-known as medicinal fungi (medicinal mushrooms) that are used in treatment of bacterial and viral infections, cancer, diabetes, and ulcer (Lee and Yun, 2011). Fungal β-(1→ 3),(1→ 6)-glucans are non-cellulosic β-glucans that are used clinically in China and Japan as potent immunological activators treating diseases like microbial infections, hypercholesterolaemia, cancer, and diabetes (Chen and Seviour, (2007).

Table 1: Fungi in medicinal importance

Name of fungi	Medicinal importance	Description	References
Larch quinine fungus *(Laricifomes officinalis)*	Astringent, Diarrhoea, Water motion, Vomiting, Haemorrhoids spasmodic coughing suppressing lactation	The active ingredient is Agricin	Vaidya and Rabba, 1993
Chaga *(Tchaga)*	Used in Ulcers , Tumours (Pulmonary and Gastric), Chronic Gastritis	Sold under the trade name "Befungin" has been approved within Russian medicinal research	Vaidya and Rabba, 1993
Snuff Fungus *(Daedaleopsis favida)*	Treatment for jaundice, Treatment of chronic diseases	Traditional medicine Mumbai (Bappa sule)	Vaidya and Rabba, 1993
Umbarache Ken	Cures Kidney disorders	Grows on fungus on ficus religiosa linn.	Vaidya and Rabba, 1993
Phansomba *(Fomes fomentarius)*	Diarrhoea and dysentery, healing of wounds	Used mostly by western Indian aqyurvedic doctors introduced into India by the Portuguese in Goa	Vaidya and Rabba, 1993

Ganoderma lucidum (Curt.: Fr.) P. Karst.	Showing anticancer and antitumor properties, treatment of hepatopathy, chronic hepatitis, nephritis, hypertension, arthritis, neurasthenia, insomnia, bronchitis, asthma, and gastric ulcers.[	Contain numerous bioactive compounds including polysaccharides, triterpenes, and immunomodulatory proteins	Chang and Buswell, 1999; Wasser, 2005

Fungi play a major role in Ayurvedic methods like Dravyaguna and pharmacognosy shows good medicinal importance in India and western countries (Vaidya and Rabba, 1993)., Fungi also plays an important role as medicinal and human food from past 30 years leads to finding population structure, climatic factors and distribution that influence the of existence of endophytic fungi grows on host plants (Jia, et al., 2016).

Ganoderma Lucidum

Ganoderma lucidum is a wood-degrading fungi that belongs to basidiomycetes is very rare in nature that has pharmacological effects (Boh et al., 2007). In Latin, lucidum means shiny or brilliant appearance on fruiting body showing a symbol of good fortune, happy augury, longevity, good health, and even immortality (Wasser, 2005). It has good therapeutic potential in the promotion of health and longevity that is used extensively as "the mushroom of immortality" in Asian countries like China, Japan, Korea and India from past 2000 years (Sanodiya et al., 2009; Sliva, 2003). The dried powder of *Ganoderma lucidum* is mostly used in the treatment of cancer in ancient China. Ganoderma lucidum, an oriental medicinal fungus (Figure 1) showing a variety of biological activities like anticancer activity (Yuen and Gohel, (2005), anti-diabetic activity (Ma, et al., 2015), hypoglycemic effect (Zhang and Lin, 2004). antimicrobial and antioxidant properties (Zhu et al., 1999; Kamra and Bhatt, 2012).

Figure 1: *Ganoderma lucidum*

Herbal medicines are important in health care systems throughout the world from ancient times of mankind that are attracting more attention within the context of health sector reform (Table 2). β-sitosterol and 5α-reductase inhibitor are well-known molecules that were identified in the Ganoderma extracts. Ganoderma is considered to be a natural medicine with clinical benefits like hepatitis, chronic bronchitis, hyperglycemia, hypertension, leucopenia, arteriosclerosis, muscular dystrophy, cancer, and hypercholesterolemia (Nahata, 2013).

Table 2: Treatment And Extraction Process F Compounds From Fungi

Compound present	Treatment	Extraction process	Reference/s
5α-reductase	Prostatic hyperplasia	Petroleum ether extract via high-performance thin-layer chromatography	Nahata and Dixit, .2012
Ganodermin	Inhibited the mycelial growth of *Fusarium oxysporum*, *Botrytis cinerea* and *Physalospora piricola*	Chromatography on DEAE-cellulose, Affi-gel blue gel, CM-Sepharose and Superdex 75.	Wang and Ng. 2006
Laccase	Human immunodeficiency Virus (HIV)-1	Sequential chromatography on DEAE-cellulose and Affi-gel blue gel and adsorption on Con A-Sepharose,.molecular mass of 75 kDa protein	Wang and Ng. 2006
Triterpenes	Antioxidant, metabolic-regulating, immunomodulatory, and anti-inflammatory activities	Methanol, ethanol, acetone, chloroform, ether, or a mixture of these solvents in normal and reverse-phase HPLC	(Chen et al. 1999; Su et al. 2001).
Ganoderic acids A and B	Prostate Cancer	Cellulose-dissolving ionic liquids	Kubota et al., 1982
Ganoderic and lucidenic acids, other triterpenes such as ganoderiols, ganoderals, and ganodermic acids	Antibacterial, antiviral, antitumor, antiosteoclastic differentiation activity, anti-HIV-1, hepatoprotection, antioxidation, antihypertension, cholesterol reduction, and antiaggregation functions.	Based on 7 fractions Column	Nishitoba et al. 1984; Sato et al. 1986; Budavari 1989;
Ethyl acetoacetate ethylene acetal Pyridine-3-ol	AgNPs synthesized using *G. lucidum* with 70%	GC–MS study	Al-Ansari et al., 2020

1,4-Dioxane-2,3-diol Butylated Hydroxy Toluene 9-Cedranone	ethanol extract inhibited the growth of *E. coli*		

The family Ganodermataceae is double-walled basidiospore fungi having 219 species. *Ganoderma* species is having different shape and color (red, white, black, yellow, blue/green, and purple) of the fruit body with host specificity, and geographical origin. The artificial cultivation of *G. lucidum* can be achieved using substrates such as grain, sawdust and wood logs in South China (Black type) and Japan (red type). *G. lucidum* contains 26–28% carbohydrate, 1.8% ash, 59% crude fiber, 3–5% crude fat, and 7–8% crude protein where as mushrooms contain 10% consists of 3–28% carbohydrate, 10–40% protein, 8–10% ash, 2–8% fat, 3–32% fiber, and some vitamins and minerals, with calcium, magnesium, potassium, phosphorus, selenium, zinc, iron, copper, terpenoids, steroids, phenols, nucleotides and their derivatives, glycoproteins, polysaccharides, peptidoglycans, and triterpenes (Wachtel et al., 2011) . *G. lucidum* in used in the treatment of cancer, diabetes, bacterial and viral infection, and liver injury.

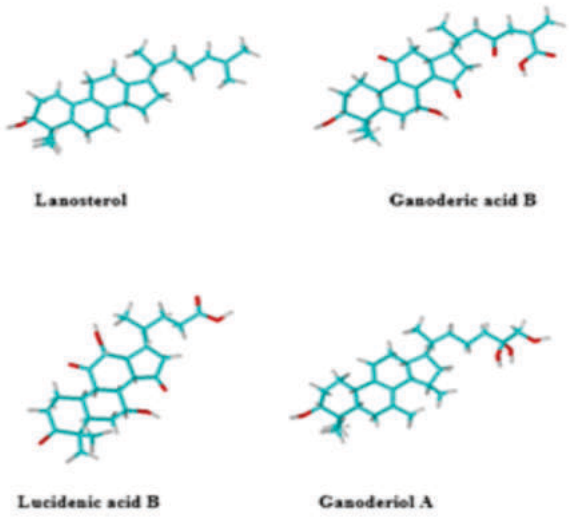

Figure 2: Compounds from *G. lucidum*

Two new lanostane-type triterpenoids, ganoderiol A (1) and ganoderiol B (2) together with known ganodermanontriol (3) and ganodermatriol (4). The compounds were identified as 5α-lanosta-7,9(11)-dien-3β,24,25,26-tetraol (1), 15α,26,27-trihydroxy-5α-lanosta-7,9(11),24-trien-3-one (2), 24,25,26-trihysdroxy-5α-lanosta-7,9(11)-dien-3-one (3) and 5α-lanosta-7,9(ll),24-trien-3β,26,27-triol (4), respectively are isolated from Ganoderma lucidum (Sato et al. 1986).

PATHOGENIC MICROBES ON HUMAN

Microbes and hosts play important interacticve mechanisms towards reciprocal relationship. Humans contain dynamic and complex community of microbes known as microbiome that processes a "metaorganism" towards pathogenic or symbiotic relationships to the host (Cho and Blaser, 2012,). Yeast and fungal proteins including (1,3)-□-glucan, high levels of fungal polysaccharides diffuse mycoses in the peripheral blood of patients that chronic fungal infections may increase risk. Composition of the human microbiome and exposure to pathogens changes with age, diet, lifestyle, and biological environment.

PATHOGENIC MICROBES IN EAR, NOSE, THROAT INFECTIONS

Staphylococcus spp, Streptococcus spp, Escherichia, Pseudomonas. are leading pathogens present on ear, nose and throat region, The common bacteria isolated from ear exudate, are ***Staphylococcus aureus*** *(45%), Pseudomonas aeruginosa (34%), Proteus mirabilis (16%)* and Other organisms, were isolated is less frequently. microorganisms can protected by extrinsic pathogenic threats (Agha and Al-Delaimi, 2021). When imbalance occurs, the organism is susceptible to a cause of infections. Synthetic drugs used to help the body fight against from fungal, bacterial, or viral burden (Table 3). They may produce undesirable consequences such as toxicity, adverse effects, and drug resistance. Therefore, research focused on developing novel formulations which is based on natural compounds for safer and more efficient alternatives. The microbiomes of the ear, nose, and throat, and pathogenic microorganisms, and related infections the mode of action of antimicrobial drugs that are used to treat those infections. A haemolytic *Streptococcus* infection. Respiratory tract infection (RTI) with followed by Staphylococcus aureus (14%), *Klebsiella pneumoniae* (11%), *Escherichia coli* (07%) and *Enterobacter cloacae* (07%) patients is considered as major health problem in Throat Infections in Lower Himalayan Region (Singh, 2020).

Table 3: Pathogenic Microbes And Infection Caused From ENT Microbes

Human Part	Pathogenic Microbes	Infection	References
Ear	*Pseudomonas aeruginosa Aspergillus niger & Candida albicans. Streptococcus pneumoniae & Haemophilus influenzae & Moraxella catarrhalis*	Swelling, inflammation , irritation, and drainage of pus and/or blood, Permanently damage the ear canal, leading to hearing loss wimmer's ear.	*Keene et al., 2004.* *Ho et al., 2006*
Nose	*S. pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis, S. aureus*	Colonize the nasal passages of healthy children. Colonization of the nasal passages is adults.	Liu et al., 2015.
Throat	*Firmicutes, Fusobacteria, Streptococcus , Neisseria, Gemella*	Pain and sensation of heat in the throat, fever, cough, congestion, flu-like symptoms, swollen lymph nodes	Hong-Li Gong et al.,2013

Staphylococcus aureus, *Pseudomonas aeruginosa*, *Proteus spp*. and *Klebsiella* spp. are leading pathogenic microbes in paediatric patients. Most of the isolates showed high resistance to some antibiotic like cephalosporins. (Abernethy *et al.,*2017). Infections remain the causes of disease, in upper respiratory infections causes hearing loss and disability of learning found in children. In developing countries, name chronic otitis-media causes serious ear infection. Otitis-media, now known to be the most common childhood infection, which leads annually death of over 50,000 children under 5 years, in nasal conditions case of nasal myiasis/ maggots in the nose.

Some Factors Affect The Diseases

1- Air pollution directly affect the nose and larynx causing

irritation, inflammation and infections, ear is also affected and causing impairment of middle ear, when pollutant enter the mucosa of the tuba.

2- Environmental pollution increasing resistance of microorganisms associated with ENT infections.

3- Emotional stress often with significant impairment of the daily life affected patients. With increase in global population.

SYNTHESIS OF ETHANOLIC AgNO3 EXTRACT OF *GANODERMA LUCIDUM*

Ganoderma lucidum was reported with rich medicinal properties due to having good number of medicinal compounds (Al-Ansari et al., 2020). Fungal bioactive compounds show potential biomedical application for alternative therapy for alimentary infections. In the present decades, there is a much gaining attention to scientists in green synthesis of silver nanoparticles (AgNPs) from plant extracts due to abundance, environmental issue and the cost-effective solution. AgNPs can be characterized by techniques like UV-Vis spectrophotometer, X-ray diffraction (XRD), FTIR, energy-dispersive X-ray spectroscopy (EDX), SEM, and transmission electron microscopy (TEM) (Nguyen et al., 2021).

BIOCHEMICAL PROPERTIES OF *Ganoderma lucidum*

Biochemical properties of mushroom fruiting bodies are numerous, and higher Basidiomycetes mushrooms have been used in folk medicine throughout the world since ancient times. *Ganoderma lucidum* reportedly has anti-inflammatory properties. TLC analysis suggested that the active principles in vivo were triterpenoids. These results indicate that the triterpenoids fraction of *G. lucidum* might be a useful ingredient in the treatment of benign prostatic hyperplasia (Table 4).

Ganoderma lucidum species is mostly using in the formulation of functional foods and as nutraceuticals. The fungi are recognized in modern and traditional medicine and pharmacology systems for the presence of biochemical compounds. The process of glycosylation of proteins plays an important role in the occurrence of biochemicals within the fungi.

BIOLOGICAL PROPERTIES OF *Ganoderma lucidum*

Antioxidant Activity

Ganoderma lucidum **is a** famous Chinese medicinal mushroom that is mostly cultivated procedurally, harvested seasonally and should be dried for preservation. Oxidative metabolism in the body is essential that are present in foodstuffs for the survival of cells (Antolovich et al., 2002). Free radical scavenging properties by ascorbic acid have many health benefits in biological systems have many important bioactive compounds showing pivotal role in delaying oxidative rancidity (Table 5).

Antimicrobial Properties

Most of the plant and mushrooms are showing medicinal properties for thousands of years for the investigations into its mode of action as antimicrobial agents (Table 6). Antioxidant antibacterial, antifungal, insecticidal and antiviral properties have been investigated in several plants**.**

X-ray Film Method

Gelatin is a natural polymer that is non toxic, biodegradable, and biocompatible. Bio-Silver nanoparticles synthesized from *Ganoderma lucidum* have lot of properties; Anti-diabetic, Anti-microbial, anti-inflammatory and wound healing properties (Sneha, 2015) . Drug that are in nano size help in easy targeted and transferred to specific site. Gelatine and bio-silver nanoparticles synthesized from *Ganoderma lucidum* are anticipated the combination effect with nanosized drug (Bio-Silver nanoparticles) compounds results may serve as promising film forming matrix for transdermal delivery of drugs into skin.

MOLECULAR MECHANISM FOR TRETMENT OF MICROBS IN EAR, NOSE, THROAT INFECTIONS

Amoxicillin is one of the most commonly used antibiotics that is effective against *Streptococcus* species, *Listeria monocytogenes, Enterococcus spp., Haemophilus influenzae*, some *Escherichia coli, Actinomyces spp., Clostridium species, Salmonella spp., Shigella spp., and Corynebacteria* species. Amoxicillin is in the class of beta-lactam antimicrobials that bind to penicillin-binding proteins that inhibit process of transpeptidation (Akhavan et al., 2021). human microbiome is a complex community with different microbial composition, function and microbial niche Specificity present in different human body sites like gastrointestinal tract, skin, and airways (Ear, Nose, Throat) (Kumpitsch et al., 2019). The oral microbiome is commonly associated with systemic diseases that can extend to surrounding tissues, spread and overgrow in the oral mucosae. Many natural compounds from plants, animals and microbes show antifungal, antibacterial, antiviral, and antibiofilm activities. Studies reveled that combining silver nanoparticles with natural extracts have also shown better promising results (Adelina-Gabriela and Alexandru, 2021).

Microbial infections of the ear, nose, and throat are common problems that are encountered by human beings practicing with treatment with antimicrobial drugs are challenging to scientists due to mechanism of resistance developed by the microorganisms (Muhammad et al., 2021). Mechanisms like disruption of the protective extrapolymer matrix, interruption of quorum sensing, inhibition of related genes, mechanical debridement of the biofilm-bearing tissues and macrolides (clarithromycin and erythromycin) are some effective prevention and management strategies in formation of Biofilms during chronic and common antibiotic-resistant during ear, nose, and throat (ENT) infections (Petros et al., 2007).

IN SILICO STUDIES OF EXTRACT OF *Ganoderma lucidum*

Medicinal fungus *Ganoderma lucidum* Karst. (Ganodermataceae) showing screening using 529 pharmacophore models and 279 compounds has been developed by Ulrike et al., 2015. Systematic isolation, and in silico pharmacological prediction has been conducted to discover potential anti-cancer activity from G. lucidum. Compounds like 3□,7□,15□-trihydroxy-11,23-dioxo-lanost-8,16-dien-26-oic acid, 3□,7□,15□-trihydroxy-11,23-dioxo-lanost-8,16-dien-26-oic acid methyl ester, (4E,8E)-N-D-2□-hydroxypalmitoyl-l-O-□-D-glucopyranosyl-9-methyl-4,8-spingodienine, ganotropic acid, 3□,7□,15□,28-tetrahydroxy-11,23-dioxo-lanost-8,16-dien-26-oic acid, (3□,7□)-dihydroxy-lanosta-8,24-dien- 11-one, 26-nor-11,23-dioxo-5□-lanost-8-en-3□,7□,15□,25-tetrol and stigmasta-7,22-dien-3□,5□,6□-triol were first reported from the genus Ganodema. The research on extraction, isolation, pharmacological prediction, and protein interaction network (PIN) analysis might be useful to predict pharmacological activities rapidly and discovery of novel compounds (Shao et al., 2016).

CONCLUSION

Most of the plant and mushrooms are showing medicinal properties for thousands of years for the investigations into its mode of action as antimicrobial agents. Antioxidant antibacterial, antifungal, insecticidal and antiviral properties have been investigated in several plants and microbes. There is a much gaining attention to scientists in green synthesis of silver nanoparticles (AgNPs) from plant extracts due to abundance, environmental issue and the cost-effective solution.

Acknowledgement:

The author would like to thank the administration of Atal Bihari Vajpayee University for providing facilities for PhD work and all the staff for their assistance.

Conflicts Of Interest:

There is no known conflict of interest associated with the publication.

REFERENCES

1. Abernethy J. R., Guy, E.A., Sheridan, S. Hopkins., M. Kiernan, M.H., Wilcox, A.P. Johnson, R. Hope, R.A. Sen, A. Mifsud, J. O'Driscoll, N. Brown, Cheryl Trundle, D. Allison, M. Twagira, Gnanarajah, F. Awad-El Kariem, R. Rajendran, S. Umashankar, G. Horne, A. Claxton, J. Cheesbrough, A. Kirby, R. Mulla, L. Teare, C. Rosmarin, G. Gopal Rao, D. Richards, T. Boswell, I. Bowler, L. O'Connor, P. Jenks, S. Wyllie, N. Virgincar, S. Hopkins, M. Dallantonia, A. Rodgers, R. Ellis, J. Bowley, M. Kiernan, K. Knox, U. Riley, M. Kelsey, P. Wilson, N. Shetty, J. Orendi, M. Pasztor. Epidemiology of Escherichia coli bacteraemia in England: results of an enhanced sentinel surveillance programme.Journal of Hospital Infection, 95(4), (2017)., 365-375,
2. Acharya, K., Bera, M., Tarafder, E., & Dasgupta, A. (2015). Pharmacognostic standardization of Ganoderma lucidum: A commercially explored medicinal mushroom. *Der Pharmacia Lettre*, *7*(7), 175-181.
3. Adelina,G. N., & Alexandru, M. G., Natural Compounds for Preventing Ear, Nose, and Throat-Related Oral Infections. Plants 2021, 10, 184
4. Agha, Z. H. M., & Al-Delaimi, M. S. (2021). Prevalence of common bacterial etiology and antimicrobial susceptibility pattern in patients with otitis media in Duhok Province–Iraq. *Zanco Journal of Pure and Applied Sciences*, *33*(4), 11-25.
5. AKANDA, M. (2013). *Phytochemical & Pharmacological Investigations of Genoderma Lucidum* (Doctoral dissertation, East West University).
6. Akhavan, BJ., Khanna, NR., Vijhani, P, Amoxicillin. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; (2021).
7. Al-Ansari, M. M., Dhasarathan, P., Ranjitsingh, A. J. A., & Al-Humaid, L. A. (2020). Ganoderma lucidum inspired silver nanoparticles and its biomedical applications with special reference to drug resistant Escherichia coli isolates from CAUTI. *Saudi Journal of Biological Sciences*, *27*(11), 2993-3002.
8. Antolovich, M., Prenzler, P. D., Patsalides, E., McDonald, S., & Robards, K. (2002). Methods for testing antioxidant activity. *Analyst*, *127*(1), 183-198.
9. Bennett, J. W. (1998). Mycotechnology: the role of fungi in biotechnology. *Journal of biotechnology*, *66*(2-3), 101-107.
10. Bharadwaj, S., Lee, K. E., Dwivedi, V. D., Yadava, U., Panwar, A., Lucas, S. J., ... & Kang, S. G. (2019). Discovery of Ganoderma lucidum triterpenoids as potential inhibitors against Dengue virus NS2B-NS3 protease. *Scientific reports*, *9*(1), 1-12.
11. Bijalwan, A.,1.,Bahuguna, K.,1.,Vasishth, A.,1., Singh, A.,1.,Chaudhary, S.,1.,Tyagi, A., 2., Thakur, MP., 3., Thakur, K., T.,4., Dobriyal, M., JR.,5., Kaushal, R.,1.,Singh, A., 2., Maithani,N., 2., Kumar, D., 1., Kothari,G., 1., Chourasia, P, K., 2., 1 .,College of Forestry, VCSG Uttarakhand University of Horticulture and Forestry, India, Insights of medicinal mushroom (Ganoderma lucidum): prospects and potential in India.
12. Boh, B., Berovic, M., Zhang, J., & Zhi-Bin, L. (2007). Ganoderma lucidum and its pharmaceutically active compounds. *Biotechnology annual review*, *13*, 265-301.
13. Budavari, S. (1989). *The Merck Index*. 11 ed, 845. New Jersey: Merck & Co., INC.
14. Celal, B. (2019). Antioxidant & antimicrobial capacities of Ganoderma lucidum. *MedCrave*, *7*(1), 5-7.
15. Chang, C. J., Lin, C. S., Lu, C. C., Martel, J., Ko, Y. F., Ojcius, D. M., Tseng SF, Wu TR, Chen YY, Young JD & Lai, H. C. (2015). Ganoderma lucidum reduces obesity in mice by modulating the composition of the gut microbiota. *Nature communications*, *6*(1), 1-19.
16. Chang, S. T., & Buswell, J., A., (1999). Ganoderma lucidum (Curt.: Fr.) P. karst.(Aphyllophoromycetideae)– a mushrooming medicinal mushroom. *International Journal of Medicinal Mushrooms*, *1*(2).
17. Chen, D., H., Shiou, W., Y., Wang, K., C., editors. et al. Chemotaxonomy of triterpenoid pattern of HPLC of Ganoderma lucidum and Ganoderma tsugae. J Chin Chem Soc. 1999;46:47–51.
18. Chen, J., & Seviour, R., (2007). Medicinal importance of fungal β-(1→ 3),(1→ 6)-glucans. *Mycological research*, *111*(6), 635-652.
19. Cho, I., & Blaser, M., J., (2012). The human microbiome: at the interface of health and disease. *Nat. Rev. Genet*. 13, 260–270.
20. De Lucca, A. J., (2007). Harmful fungi in both agriculture and medicine. *Revista iberoamericana de micología*, *24*(1), 3.
21. El Mansy, SM., (2019). Postgraduate student at Zoology Department, Faculty of Science, Suez Canal University, Ismailia 45122, Egypt, Ganoderma : The mushroom of immortality. Microbial Biosystems 4(1), 45-57.
22. Elumalai, D., Suman, T., Y., Hemavathi, M., Swetha, C., Kavitha, R., Arulvasu, C., & Kaleena, P. K. (2021). Biofabrication of gold nanoparticles using Ganoderma lucidum and their cytotoxicity against human colon cancer cell line (HT-29). *Bulletin of Materials Science*, *44*(2), 1-6.
23. Fahselt, D., (1994). Secondary biochemistry of lichens. Symbiosis 16, 117D165.
24. Grienke, U., Mihály-Bison, J., Schuster, D., Afonyushkin, T., Binder, M., Guan, S. H., & Rollinger, J. M. (2011). Pharmacophore-based discovery of FXR-agonists. Part II: identification of bioactive triterpenes from Ganoderma lucidum. *Bioorganic & medicinal chemistry*, *19*(22), 6779-6791.
25. Gupte, A., Palande, A., Venkata, S., & Pol, R. (2018). Docking Studies of Ganoderma Lucidum. *International Journal of Pharmaceutical Sciences and Research*, *9*(3).
26. Hexiang, W., & T.B. Ng. Ganodermin, an antifungal protein from fruiting bodies of the medicinal mushroom Ganoderma lucidum. Peptides, 27(1), 2006, 27-30,
27. Ho, T., Vrabec, J. T., Yoo, D., & Coker, N. J. (2006). Otomycosis: clinical features and treatment implications. Otolaryngology—Head and Neck Surgery, 135(5), 787-791.
28. Hong-Li Gong, Yi Shi, Liang Zhou, Chun-Ping Wu, Peng-Yu Cao, Lei Tao, Chen Xu, Dong-Sheng Hou, Yue-Zhu Wang, (2013). The Composition of Microbiome in Larynx and the Throat Biodiversity between Laryngeal Squamous Cell Carcinoma Patients and Control Population: e66476. Published online 2013 Jun 18. doi: 10.1371/journal.
29. Indumathi, M., S Smiline Girija, A., Sankar Ganesh, P., & Vijayashree Priyadharsini, J. (2021). Detection of Immuno Dominant Peptides against pgaB of Acinetobacter baumannii.
30. Jia, M., Chen, L., Xin, H. L., Zheng, C. J., Rahman, K., Han, T., & Qin, L. P. (2016). A friendly relationship between endophytic fungi and medicinal plants: a systematic review. *Frontiers in microbiology*, *7*, 906.
31. Kamra, A., & Bhatt, A. B. (2012). Evaluation of antimicrobial and antioxidant activity of Ganoderma lucidum extracts against human pathogenic bacteria. *International journal of pharmacy and pharmaceutical sciences*, *4*(2), 359-362.
32. Kapoor, P., & Sharma, B. M. (2014). Studies on different growth parameters of Ganoderma lucidum. *Int J Sci Environ Tech*, *3*, 1515-1524.
33. Keene WE, Markum AC, Samadpour M., Outbreak of Pseudomonas aeruginosa Infections Caused by Commercial Piercing of Upper Ear Cartilage. JAMA. (2004);291(8):981–985.
34. Kubota T, Asaka Y, Miura I, Mori H. Structures of ganoderic acids A and B, two new lanostane type bitter triterpenes from Ganoderma lucidum (Fr.) Karst. Helv Chim Acta. (1982);65:611–9.
35. Kubota, T., Y. Asaka, I. Miura, & H. Mori. (1982). *Helv Chim Acta* 65:611–9; Nishitoba, T., H. Sato, T. Kasai, H. Kawagishi, & S. Sakamura. (1984). *Agric Biol Chem* 48:2905–7;
36. Kumpitsch, C., Koskinen, K., Schöpf, V. & Christine Moissl-Eichinge The microbiome of the upper respiratory tract in health and disease. *BMC Biol* **17,** 87 (2019).
37. Lee, I. K., & Yun, B. S. (2011). Styrylpyrone-class compounds from medicinal fungi Phellinus and Inonotus spp., and their medicinal importance. *The Journal of antibiotics*, *64*(5), 349-359.
38. Li, C., Shi, L., Chen, D., Ren, A., Gao, T., & Zhao, M. (2015). Functional analysis of the role of glutathione peroxidase (GPx) in the ROS signaling pathway, hyphal branching and the regulation of ganoderic acid biosynthesis in Ganoderma lucidum. *Fungal Genetics and Biology*, *82*, 168-180.
39. Li, X., Xie, Y., & Yang, B. B. (2018). Characterizing novel anti-oncogenic triterpenoids from ganoderma. *Cell cycle*, *17*(5), 527-528.
40. Lin, M. S., Yu, Z. R., Wang, B. J., Wang, C. C., Weng, Y. M., & Koo, M. (2015). Bioactive constituent characterization and antioxidant activity of Ganoderma lucidum extract fractionated by supercritical carbon dioxide. *Sains Malays*, *44*(12), 1685-1691.
41. Liu CM, Price LB, Hungate BA, Abraham AG, Larsen LA, Christensen K, et al. *Staphylococcus aureus* and the ecology of the nasal microbiome. *Sci Adv*. (2015).
42. Liu, J., Shimizu, K., Konishi, F., Noda, K., Kumamoto, S., Kurashiki, K., & Kondo, R. (2007). Anti-androgenic activities of the triterpenoids fraction of Ganoderma lucidum. *Food Chemistry*, *100*(4), 1691-1696.
43. Ma, H. T., Hsieh, J. F., & Chen, S. T. (2015). Anti-diabetic effects of Ganoderma lucidum. *Phytochemistry*, *114*, 109-113.
44. Manzoor-ul-Haq, V. R., Singh, D., Singh, A. K., Ninganagouda, S., & Hiremath, J. (2015). Dried mushroom Agaricus bisporus mediated synthesis of silver nanoparticles from Bandipora District (Jammu & Kashmir) and their efficacy against methicillin resistant Staphylococcus aureus (MRSA) strains. *Nanosci. Nanotechnol. Int. J*, *5*, 1-8.
45. Marill, Keith A., R. Kulkarni, and P. Huff. Vestibular neuronitis. Retrieved 2008-06-28, 2011
46. Muhammad Zeeshan Ahmed, Zeeshan Mutahir, Tazeen Rao, Arshad Islam, Nayyab Hameed. Saifullah Shakeel, Haseeba Shahzad, Mazhar Ali, Shahzeb Hameed, Syed Hizbullah, Saeed Ur Rahman. (2021) Drug Resistance in Ear, Nose, and Throat Infections. In: Ahmed S., Chandra Ojha S., Najam-ul-Haq M., Younus M., Hashmi M.Z. (eds) Biochemistry of Drug Resistance. Springer, Cham.
47. Muthusamy, M., K., P., Venkatachalam U, Rajarajeshwaran J(2014), Mycosynthesis, Characterization and Antibacterial activity of Silver Nanoparticles (Ag-NPs) from fungus Ganoderma lucidum, Malaya Journal of bioscience 2014, 1(3):134-142.
48. Nahata, A. (2013). Ganoderma lucidum. *A Potent Medicinal Mushroom with Numerous Health Benefits Pharmaceut Anal Acta*, *4*(10), 1000e159.
49. Nahata, A., & Dixit, V. K. (2012). Ganoderma lucidum is an inhibitor of testosterone-induced prostatic hyperplasia in rats. *Andrologia*, *44*, 160-174.
50. Nguyen, V. P., Le Trung, H., Nguyen, T. H., Hoang, D., & Tran, T. H. (2021). Synthesis of biogenic silver nanoparticles with eco-friendly processes using Ganoderma lucidum extract and evaluation of their theranostic applications. *Journal of Nanomaterials*, *2021*.
51. Nishitoba T, Sato H, Kasai T, Kawagishi H, Sakamura S. New bitter C27 and C30 terpenoids from fungus Ganoderma lucidum (Reishi). Agric Biol Chem. 1984;48:2905–7
52. Oliveira, M., Reis, F. S., Sousa, D., Tavares, C., Lima, R. T., Ferreira, I. C., & Vasconcelos, M. H. (2014). A methanolic extract of Ganoderma lucidum fruiting body inhibits the growth of a gastric cancer cell line and affects cellular autophagy and cell cycle. *Food & function*, *5*(7), 1389-1394.
53. Pan, D., Zhang, D., Wu, J., Chen, C., Xu, Z., Yang, H., & Zhou, P. (2014). A novel proteoglycan from Ganoderma lucidum fruiting bodies protects kidney function and ameliorates diabetic nephropathy via its antioxidant activity in C57BL/6 db/db mice. *Food and chemical toxicology*, *63*, 111-118.
54. Paul, S., Changam, S., Cherian, S., M., & Cheria, K., M., (2015). Biomedical evaluation of Chitosan-Gelatin transdermal patch embedded with bio-siver nanpparticles as a wound dressing material: An in vitro study. International journal of ChemTech research, 7(2), 740-746.
55. Petros V. Vlastarakos, Thomas P. Nikolopoulos , Paul Maragoudakis , Antonios Tzagaroulakis , Eleftherios Ferekidis. Biofilms in Ear, Nose, and Throat Infections: How Important are They?. 117(4), 2007, 668-67
56. Quereshi, S., Pandey, A. K., & Sandhu, S. S. (2010). Evaluation of antibacterial activity of different Ganoderma lucidum extracts. *J Sci Res*, *3*, 9-13.

57. Rakhee, shethy N, Bhardwaj A, Singh V, Sharma R, Deshwal R, Bhargava K, Mishra K(2017), characterization of ganoderma lucidum: Phytochemical and Proteomic approach. Journal of proteins and proteomics 8(1),2017,pp.25-33.
58. Rangsinth, P., Sillapachaiyaporn, C., Nilkhet, S., Tencomnao, T., Ung, A. T., & Chuchawankul, S. (2021). Mushroom-derived bioactive compounds potentially serve as the inhibitors of SARS-CoV-2 main protease: An in silico approach. *Journal of traditional and complementary medicine*, *11*(2), 158-172.
59. Rawat A, Mohsin M, Shah A.N., Negi P.S. Singh S,(2012) , Biochemical esimation of wildly collected Ganoderma lucidudm from Central Himalayan Hills of India. Pelagia Research Library Advances in Applied Science Research, 2012, 3 (6):3708-3713,
60. Saltarelli, R., Ceccaroli, P., Buffalini, M., Vallorani, L., Casadei, L., Zambonelli, A., Iotti, M., Badalyan, S. & Stocchi, V., (2015). Biochemical characterization and antioxidant and antiproliferative activities of different Ganoderma collections. *Journal of molecular microbiology and biotechnology*, *25*(1), pp.16-25.
61. Saltarelli, R., Ceccaroli, P., Iotti, M., Zambonelli, A., Buffalini, M., Casadei, L., Vallorani, L. and Stocchi, V., (2009). Biochemical characterisation and antioxidant activity of mycelium of Ganoderma lucidum from Central Italy. *Food Chemistry*, *116*(1), pp.143-151.
62. Saltarelli, R., Palma, F., Gioacchini, A. M., Calcabrini, C., Mancini, U., De Bellis, R., & Potenza, L. (2019). Phytochemical composition, antioxidant and antiproliferative activities and effects on nuclear DNA of ethanolic extract from an Italian mycelial isolate of Ganoderma lucidum. *Journal of ethnopharmacology*, *231*, 464-473.
63. Sanodiya, B. S., Thakur, G. S., Baghel, R. K., Prasad, G. B. K. S., & Bisen, P. S. (2009). Ganoderma lucidum: a potent pharmacological macrofungus. *Current pharmaceutical biotechnology*, *10*(8), 717-742.
64. Sato, H., Nishitoba, T., Shirasu, S., Oda, K., & Sakamura, S. (1986). Ganoderiol A and B, new triterpenoids from the fungus Ganoderma lucidum (Reishi). *Agricultural and biological chemistry*, *50*(11), 2887-2890.
65. Scherlach, K., Graupner, K., & Hertweck, C. (2013). Molecular bacteria-fungi interactions: effects on environment, food, and medicine. *Annual review of microbiology*, *67*, 375-397.
66. Shao, Y.; Qiao, L.; Wu, L.; Sun, X.; Zhu, D.; Yang, G.; Zhang, X.; Mao, X.; Chen, W.; Liang, W.; Zhang, Y.; Zhang, L.Structure Identification and Anti-Cancer Pharmacological Prediction of Triterpenes from Ganoderma lucidum. Molecules(2016)., 21, 678
67. Si, J., Meng, G., Wu, Y., Ma, H. F., Cui, B. K., & Dai, Y. C. (2019). Medium composition optimization, structural characterization, and antioxidant activity of exopolysaccharides from the medicinal mushroom Ganoderma lingzhi. *International journal of biological macromolecules*, *124*, 1186-1196.
68. Singh, M., Study of Infective Profile of Patients with Throat Infections in Lower Himalayan Region. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), Volume 19, Issue 2 Ser.17 (February. 2020), PP 60-64.
69. Singh, S., Kuca, K., & Kalia, A. (2020). Alterations in Growth and Morphology of Ganoderma lucidum and Volvariella volvaceae in Response to Nanoparticle Supplementation. *Mycobiology*, *48*(5), 383-391.
70. Sliva, D. (2003). Ganoderma lucidum (Reishi) in cancer treatment. *Integrative cancer therapies*, *2*(4), 358-364.
71. Su C. H, Yang Y. Z, Ho H, Hu C. H. & Sheu M. T. (2001). High-performance liquid chromatographic analysis for the characterization of triterpenoids from Ganoderma. *J Chromatogr Sci*. 39:93–100.
72. Taofiq, O., Heleno, S. A., Calhelha, R. C., Alves, M. J., Barros, L., González-Paramás, A. M., ... & Ferreira, I. C. (2017). The potential of Ganoderma lucidum extracts as bioactive ingredients in topical formulations, beyond its nutritional benefits. *Food and Chemical Toxicology*, *108*, 139-147.
73. Ulrike G., Teresa K., Florian P., Christina E. M., Thierry L., Daniela S. & Judith M. R (2015), Accessing biological actions of Ganoderma secondary metabolites by in silico profiling, *Phytochemistry*, 114, 114-124.
74. Vaidya, J. G., & Rabba, A. S. (1993). Fungi in folk medicine. *Mycologist*, *7*(3), 131-133.
75. Wachtel-Galor, S., Buswell, J. A., Tomlinson, B., & Benzie, I. F. (2004). Lingzhi polyphorous fungus (Ganoderma lucidum). In *Herbal and Traditional Medicine* (pp. 169-213). CRC Press.
76. Wachtel-Galor, W. S., Yuen, J., Buswell, J., A., & Benzie, I. F. F., Ganoderma lucidum (Lingzhi or Reishi): A Medicinal Mushroom. In: Benzie IFF, Wachtel-Galor S, editors. Herbal Medicine: Biomolecular and Clinical Aspects. 2nd edition. Boca Raton (FL): CRC Press/Taylor & Francis; (2011). Chapter 9.
77. Wang, G., Xu, L., Yu, H., Gao, J., & Guo, L. (2019). Systematic analysis of the lysine succinylome in the model medicinal mushroom Ganoderma lucidum. *BMC genomics*, *20*(1), 1-12.
78. Wasser, S. P. (2005). Reishi or ling zhi (Ganoderma lucidum). *Encyclopedia of dietary supplements*, *1*, 603-622.
79. Wong, K. L., Chao, H. H., Chan, P., Chang, L. P., & Liu, C. F. (2004). Antioxidant activity of sGanoderma lucidum in acute ethanol-induced heart toxicity. *Phytotherapy Research*, *18*(12), 1024-1026.
80. Wu, F. S., Li, Z. Q., Chen, X. Y., Lian, Z. P., Lu, S. J., & Hou, E. C. (2020). Molecular docking and big-data bioinformatics predict the mechanisms of action of the active ingredients of Ganoderma lucidum in treating lung cancer. *TMR Cancer*, *4*(1), 4.
81. Yuen, J. W., & Gohel, M. D. I. (2005). Anticancer effects of Ganoderma lucidum: a review of scientific evidence. *Nutrition and cancer*, *53*(1), 11-17.
82. Zeng, P., Guo, Z., Zeng, X., Hao, C., Zhang, Y., Zhang, M., Liu, Y., Li, H., Li, J. & Zhang, L., (2018). Chemical, biochemical, preclinical and clinical studies of Ganoderma lucidum polysaccharide as an approved drug for treating myopathy and other diseases in China. *Journal of cellular and molecular medicine*, *22*(7), 3278-3297.
83. Zeng, X., Li, P., Chen, X., Kang, Y., Xie, Y., Li, X., Xie, T. and Zhang, Y., (2019). Effects of deproteinization methods on primary structure and antioxidant activity of Ganoderma lucidum polysaccharides. *International journal of biological macromolecules*, *126*, pp.867-876.
84. Zhang, H. N., & Lin, Z. B. (2004). Hypoglycemic effect of Ganoderma lucidum polysaccharides. *Acta Pharmacologica Sinica*, *25*(2), 191-195.
85. Zhang, H. N., & Lin, Z. B. (2004). Hypoglycemic effect of Ganoderma lucidum polysaccharides. *Acta Pharmacologica Sinica*, *25*(2), 191-195.
86. Zhu, L. F., Yao, Z. C., Ahmad, Z., Li, J. S., & Chang, M. W. (2018). Synthesis and evaluation of herbal chitosan from Ganoderma lucidum spore powder for biomedical applications. *Scientific reports*, *8*(1), 1-12.
87. Zhu, M., Chang, Q., Wong, L. K., Chong, F. S., & Li, R. C. (1999). Triterpene antioxidants from Ganoderma lucidum. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, *13*(6), 529-531.