EXPLORING THE POTENTIAL OF GANODERMA LUCIDUM IN CANCER TREATMENT: BENEFITS AND LIMITATIONS OF ITS BIOLOGICAL ACTIONS

Ganoderma lucidum's therapeutic potential and challenges in the treatment of cancer

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***Abstract*— Ganoderma lucidum, a traditional Asian medicine with a long history, has been found to be a potential candidate in complementary cancer therapy. This review thoroughly discusses the anticancer potential of G. lucidum based on its bioactive compounds, mainly polysaccharides and triterpenoids, and their mechanistic functions. The mushroom has multifunctional activities, such as immune system modulation, apoptosis induction, cancer cell proliferation inhibition, metastasis and angiogenesis suppression, and oxidative stress regulation. Polysaccharides activate immune cells and cytokine production, which increases the host's antitumor activity. Triterpenoids, especially ganoderic acids, have direct cytotoxicity and modulate pathways like PI3K/Akt and MAPK. G. lucidum exerts synergistic action with chemotherapy and radiotherapy, enhancing the efficacy of treatments and minimizing side effects such as nausea and fatigue. In spite of its therapeutic potential, limitations including low bioavailability, unstandardized extract, and insufficient high-quality clinical trials limit its clinical use in the mainstream. Future studies must be directed towards nanoparticle-based drug delivery systems and standardized formulations to enhance efficacy and predictability. This review underscores the great potential of G. lucidum as both a treatment and prophylactic agent in oncology, which deserves further investigation and clinical testing.**

***Key Words* — Ganoderma lucidum, cancer therapy, triterpenoids, PI3K/Akt**

Introduction:

1.1. Ganoderma lucidum

Ganoderma lucidum, or Lingzhi in Chinese and Reishi in Japanese, has two millennia of history. Its medicinal fungus use is deeply rooted in Asian cultures, especially in China, where it is highly prized for its purported health benefits. G. lucidum is initially described in the Shen Nong Ben Cao Jing (Classic of Materia Medica), written during the Eastern Han period (25-220 AD). This seminal treatise categorized numerous plants and their healing virtues, of which G. lucidum was one of the most highly valued because of its supposed ability to enhance longevity and energy [1,3]. G. lucidum has been a part of Taoism for centuries, featuring in various forms of art and literature as a representation of immortality and spiritual strength. Its images were often depicted with gods, showing its high status in religious practices [1-2]. The mushroom was scarce and costly in the past, and only the rich could afford it. Its rarity made it gain a reputation as a panacea for ailments, solidifying its position in traditional medicine's cultural heritage.

G. lucidum is traditionally referred to as the "herb of spiritual power" in Chinese society, symbolizing concepts of success, health, and divine power. The name "Lingzhi" by itself conveys connotations with longevity and health. This cultural value is not only limited to China; equal esteem is observed in Japan and other parts of Asia where G. lucidum is integrated into many healing arts [1,2,4]. The value of the mushroom in traditional medicine is not confined to folklore; it is documented in many classical texts throughout history. For instance, the Ben Cao Gang Mu, written by Li Shizhen in the Ming dynasty (1590 AD), discusses at length its therapeutic potential, including its effect on vital energy (Qi), memory, and anti-aging benefits [1,4]. These accounts from history reflect a widespread belief in the mushroom's ability to enhance overall health and longevity.

Ganoderma lucidum is a member of the Basidiomycota phylum of the Ganodermataceae family. It differs from other food mushrooms because of its unique shiny appearance and woody texture. The name "Ganoderma" comes from Greek words meaning "shining skin," which adequately characterize the shiny top of the mushroom [3]. Increased need for G. lucidum medicinal properties has resulted in changing cultivation from wild harvesting to mass cultivation. Today, a variety of commercial forms are available, such as in the form of tinctures, teas, capsules, and other preparations in the form of the mycelium, spores, and fruiting bodies of the fungus [1-2]. This commercialization is a testament to its modern-day application in health and wellness as well as its traditional significance.

In recent decades, Ganoderma lucidum has gained renewed attention in both contemporary scientific research and traditional practices. Beyond its conventionally acknowledged health benefits, G. lucidum has garnered attention as people look for natural alternatives to conventional medicine. Many of the old claims about this mushroom are starting to be supported by new research, which is looking into its uses in a number of health areas, such as stress management and immunological modulation [2-3].

Figure: 1 Ganoderma Lucidum

1.2. Importance in cancer therapy:

Increasing awareness of the potential benefits of the use of natural products along with conventional therapies for cancer is the motivation for the heightened interest in these products across the globe. To enhance the outcome of treatments or their quality of life without suffering from the adverse side effects that are commonly associated with chemotherapy and radiation, most patients seek complementary therapies [4-5]. Notably, Ganoderma lucidum has attracted interest owing to its purported anticancer and immunoenhancing properties.

Based on studies, G. lucidum extracts are able to inhibit tumour growth through various mechanisms, including the modulation of immune response and direct cytotoxicity against cancer cells. Polysaccharides and triterpenes derived from this fungus have been reported in laboratory studies to possess strong anticancer properties against a wide range of cancer cell [4-6]. G. lucidum is also frequently used as an adjuvant therapy by cancer patients to enhance their immune systems during chemotherapy [1,4].

2. PHYTOCHEMICAL COMPOSITION OF GANODERMA LUCIDUM

2.1. Key bioactive compounds

The medicinal mushroom, Ganoderma lucidum, is renowned for its diversified bioactive chemicals responsible for its medicinal properties. Among the most critical bioactive components include polysaccharides, triterpenoids, proteins, sterols, and many more that in combination have conferred numerous health benefits, with some of them particularly exhibiting anti-cancer activity.

2.1.1. Polysaccharides:

Polysaccharides are one of the most intensively studied components of G. lucidum. These complex carbohydrates are composed of glucose mostly, and may contain xylose, mannose, and galactose. The following is the list of main polysaccharides in G. lucidum:

Beta-glucans are known to have immune-modulating activity and are an essential component of strengthening the body's cancer-fighting mechanisms. Beta-glucans stimulate macrophages and natural killer cells, which are needed to detect and destroy cancer cells [1,7].

Antioxidant Properties: Polysaccharides in G. lucidum have significant antioxidant activity, helping to neutralize free radicals and minimize oxidative stress, which is a critical role in cancer development [8-9].

Anti-diabetic Effects: Some polysaccharides act as anti-diabetic agents by lowering blood glucose levels and improving insulin sensitivity [8].

Research reveals that polysaccharides isolated from G. lucidum can suppress tumour growth and increase the proliferation of immune cells, leading to its anticancer benefits [7-8].

2.1.2. Triterpenoids:

Triterpenoids constitute another significant category of bioactive compounds found in G. lucidum, with more than 150 different types identified. Significant triterpenoids include:

Ganoderic acids: At low concentrations, these compounds have been reported to exert potent cytotoxic activities against numerous human cancer cell lines. They induce apoptosis (programmed cell death) in cancer cells and hence inhibit tumour growth [7,9,10].

Anti-inflammatory Properties: Triterpenoids also have anti-inflammatory properties because they modulate inflammatory pathways, which can help prevent cancer-related inflammation [8-9].

Regulation of Cholesterol: Certain triterpenoids have been proven to reduce levels of cholesterol, which aids cardiovascular health as well as their anticancer activity [8,10].

2.1.3. Proteins and Peptides:

G. lucidum contains a number of proteins and peptides that contribute to its therapeutic properties:

LZ-8 Protein: This immunosuppressive protein was isolated from G. lucidum mycelia and is considered to play a role in immune response modulation [1].

Hepatoprotective Peptides: Certain peptide formulations obtained from G. lucidum have hepatoprotective and antioxidant properties, making them advantageous to liver health [1,10].

Antifungal Proteins: Ganodermin is a notable antifungal protein extracted from the fruiting bodies of G. lucidum, showing its potential to cure fungal infections [1].

2.1.4. Sterols:

G. lucidum has sterols that make it have such health impacts:

Ergosterol is a precursor to vitamin D2, has been linked to a variety of biological functions, including antioxidant properties [7,10].

Ergosterol Peroxide is sterol has exhibited significant anti-cancer activity in vitro against various cancer cell lines, suggesting its therapeutic potential [7].

2.2. Mechanistic importance:

Recent years have seen increased attention in Ganoderma lucidum due to potential antitumor activities. The mechanisms through which its bioactive compounds act to cause these effects are complex and diverse. This chapter reviews the molecular significance of G. lucidum's major bioactive constituents, mainly polysaccharides and triterpenoids, in relation to anticancer activity.

2.2.1. Polysaccharides:

Polysaccharides in G. lucidum represent one of the major active constituents, especially in water-soluble extracts. The mechanisms of their antitumor activities include:

Immunomodulation: The polysaccharides stimulate many immune cells like macrophages, natural killer (NK) cells, and T lymphocytes, thus making the immune system more responsive to the presence of cancer cells, thereby enhancing recognition and elimination processes [12-13]. For example, it has been demonstrated that some polysaccharides can raise the levels of various cytokines such as interleukin-2 (IL-2) and tumour necrosis factor-alpha (TNF-α) that are crucial for mediating anti-tumour immunity.

Inhibition of Cell Proliferation: Polysaccharides of G. lucidum were shown to be capable of inhibiting the proliferation of various cancer cell lines. These polysaccharides could induce cell cycle arrest by downregulating cyclin D1 and other proteins associated with cell division, thereby preventing the uncontrolled multiplication of cancer cells [13-14].

Induction of Apoptosis: Polysaccharides exhibit pro-apoptotic effects by modulation of the pathways of apoptosis. They may induce higher expression of pro-apoptotic proteins, like Bax, and decrease anti- apoptotic proteins such as Bcl-2, thereby resulting in programmed cell death in cancer cells [13-14]. It has been found that polysaccharides cause apoptosis in lung and colorectal cancer cells by these mechanisms.

Anti-Metastatic Effects: Polysaccharides were also shown to inhibit metastasis by interfering with cell adhesion and migration. They can inhibit proteins involved in EMT that is a requirement for cancer cells to metastasize [12-13]. In the process of inhibition of pathways of cell motility, polysaccharides would prevent the invasion of cancer into other tissues.

Anti-angiogenic activity: Polysaccharides have been reported to inhibit VEGF expression, thus preventing angiogenesis responsible for tumor growth by limiting the development of new blood vessels, nutritional supply, and overall survival of the tumor, eventually curtailing further growth and metastasis [13-14].

2.2.2. Triterpenoids:

Another important class of bioactive compounds of G. lucidum is triterpenoids, which possess significant anti-cancer activity:

Cytotoxic Effects: Triterpenoids, including ganoderic acid, have cytotoxic activity through induction of apoptosis and inhibition of cancer cell growth. They induce caspase cascades and inhibit mitochondrial function, hampering energy production critical for cancer cell survival and growth.

Regulation of Signalling Pathways: Triterpenoids act on several cellular signaling pathways implicated in cancer. They can suppress the PI3K/Akt pathway, which is overactivated in many cancers, thus attenuating survival signals in cells. In addition, they may interfere with the MAPK pathway responsible for cell growth and differentiation [11,15].

Anti-Inflammatory Properties: Chronic inflammation is known to be a contributing factor to cancer development. Triterpenoids have anti-inflammatory properties that help reduce this risk by suppressing inflammatory cytokines and pathways. This effect not only reduces tumorigenesis but also enhances overall immune function [14-15].

3. MECHANISMS OF ANTI-CANCER ACTION

3.1. Induction of apoptosis:

Induction of apoptosis, or programmed cell death, is an important mechanism by which Ganoderma lucidum (G. lucidum) exerts its anti-cancer effects. This process involves a series of biochemical events leading to characteristic cellular changes and death, which can be triggered by various bioactive compounds found in G. lucidum, such as triterpenes and polysaccharides.

Mechanisms of Apoptosis Induction

3.1.1. Mitochondrial Pathway Activation:

Ganoderma lucidum compounds modulate the mitochondrial apoptosis pathway by suppressing anti- apoptotic proteins such as Bcl-2. Such suppression causes disruption in mitochondrial membrane integrity, enabling cytochrome c to pass into the cytosol and activate caspase-3, inducing apoptosis. For example, Fudan-Yueyang-Ganoderma lucidum (FYGL) potently suppressed Bcl-2 expression in pancreatic cancer cells, enhancing reactive oxygen species (ROS) levels and cell death through the caspase cascade. [16].

3.1.2. Caspase Activation:

The cysteine proteases caspases are an important part of the execution phase of apoptosis. The activation of caspase-3 has been critical in this process as it results in the cleavage of several substrates that are involved in the disassembly of the cell. Studies involving treatment with G. lucidum have shown dose- dependent increases in caspase-3 activity, indicating compounds promote apoptosis by activating this pathway [17].

3.1.3. Role of Reactive Oxygen Species (ROS):

The generation of ROS is another significant pathway in the apoptosis induced by G. lucidum. Enhanced ROS causes oxidative stress, which damages cellular components and influences apoptotic pathways. In pancreatic cancer cells treated with FYGL, increased ROS levels were observed in conjunction with the reduced mitochondrial membrane potential responsible for cell death [16]. Moreover, ROS activates SAPKs that enhance the process of apoptosis.

3.1.4. Autophagy and Apoptosis Crosstalk:

Autophagy is a cellular degradative process that can promote survival or induce cell death based on context. Ganoderma lucidum extracts have been found to impair autophagic flux, leading to autophagosome accumulation that can result in apoptosis rather than cell survival. For instance, Ganoderma lucidum polysaccharides (GLP) caused autophagosome accumulation and apoptosis in colorectal cancer cells[18]. Such impairment prevents the clearance of impaired organelles, thus increasing apoptotic signalling and leading to cancer cell death.

3.1.5. Gene Expression Modulation:

The bioactive compounds in G. lucidum also control the expression of different genes, which are involved in apoptosis. For example, investigations have indicated that the extracts treat the expression of anti-apoptotic genes such as Bcl-2 and pro-apoptotic genes including Bax and p53. Such a gene expression modification supports the apoptotic process [17].

3.2. Anti-proliferative effects:

The anti-proliferative effects of Ganoderma lucidum, G. lucidum, are of significant interest in cancer therapy because the mushroom has been reported to inhibit the proliferation of various cancer cell lines through multiple mechanisms. These mechanisms include cell cycle arrest, cyclin modification, and the induction of apoptosis.

Mechanisms of anti-proliferation

3.2.1. Cell Cycle Arrest:

Ganoderma lucidum can cause cell cycle arrest, especially in G1 and G2/M phases, by suppressing cyclin D1 and cyclin B, crucial promoters of cell cycle progression. In PC-3 prostate cancer cells, extracts of G. lucidum induced deep G2/M arrest, hence preventing cell proliferation and tumor growth. [19].

3.2.2. Cyclin and CDK phosphorylation:

G. lucidum's bioactive compounds, including triterpenes, have been shown to modulate cell cycle regulators. G. lucidum effectively slows or stops cell division by upregulating p21, a cyclin-dependent kinase inhibitor, and downregulating cyclin-dependent kinases (CDKs). This mechanism is important because it prevents cancer cells from multiplying out of control [20].

3.2.3. Apoptosis induction

G. lucidum directly prevents cell proliferation and induces apoptosis in cancer cells, thus adding another anti-proliferative activity. The presence of apoptosis is usually accompanied by the upregulation of pro- apoptotic proteins, including Bax, and a down-regulation of anti-apoptotic proteins like Bcl-2. This leads to the enhancement of apoptotic signalling pathways that causes apoptosis [21].

3.2.4. Cytotoxicity:

G. lucidum extracts have been found to have a dose dependent cytotoxic effect on different cancer cell lines such as leukemic cells and gastric carcinoma cells. The IC50 data obtained indicated that the survival of cells was significantly reduced by very low concentrations of G. lucidum extracts, which confirms the potential effectiveness of this drug against carcinoma [22].

3.3. Inhibition of metastasis and angiogenesis:

3.3.1. Inhibition of metastasis

Metastasis is the process of spreading cancer cells to remote areas. Ganoderma lucidum has been demonstrated to inhibit cancer cell invasiveness, especially in breast cancer, by suppressing specific proteins such as uPA and uPAR. Inhibition of these proteins interferes with cell adhesion, migration, and invasion and, in turn, diminishes the total metastatic capacity of cancer cells [23-24].

More specifically, triterpenes extracted from G. lucidum have been found to inhibit the activity of NF- kappaB and AP-1 transcription factors in regulating genes involved in metastasis. Inhibition of these pathways limits the expression of proteins promoting cell motility and invasion, thus limiting the spread of cancer cells [20,25]

3.3.2. Inhibition of Angiogenesis

Angiogenesis or the development of new blood vessels is crucial for tumor growth and spread. Ganoderma lucidum has anti-angiogenic activity by reducing pro-angiogenic factors such as VEGF, a central mediator of blood vessel formation. This suppresses the nutrient and oxygen delivery to tumors. G. lucidum also augments immune-mediated destruction of tumor-associated blood vessels, which further impedes angiogenesis. This bimodal activity not only inhibits cancer cell growth but also debilitates the tumor microenvironment, which becomes less conducive to cancer growth and dissemination. [27-28].

3.4. Immunomodulation

Mechanisms of Immunomodulation:

3.4.1. Enhancement of Immune Cell Activity:

G. lucidum has been demonstrated to enhance the activity of several immune cells, such as T lymphocytes, natural killer (NK) cells, and macrophages. For example, it has been reported that G. lucidum extracts can enhance the proliferation and cytotoxicity of NK cells, which are crucial for the killing and destruction of tumour cells [29-30].

3.4.2. Cytokine Production:

The mushroom stimulates the production of important cytokines, including interleukin-2 (IL-2), which is essential for T-cell activation and proliferation. This cytokine release enhances both humoral and cellular immune responses, thereby improving the overall immune defence mechanism against infections and tumors [29-31].

3.4.3. Regulation of Immune Signaling Pathways:

G. lucidum impacts most signaling pathways responsible for immunomodulation, such as the TLR4/MyD88/NF-κB signaling pathway. By the regulation of these pathways, G. lucidum may augment the immunity in responding to pathogens as well as cancer cells along with anti-inflammatory effects [32].

3.4.4. Improvement of Immune Cell Ratios:

There are improvements in the CD4/CD8 T-cell ratio and increased NK cells counts with G. lucidum extract supplementation compared to the placebo group in clinical studies. This implies a more active and balanced immune response [29].

3.5. Oxidative stress regulation:

Ganoderma lucidum plays an important role in regulating oxidative stress, which is an imbalance between reactive oxygen species (ROS) production and the body's ability to detoxify these harmful compounds. This is capable of causing cellular damage and is associated with different diseases, such as cancer and neurodegenerative disorders.

Mechanisms of Action

3.5.1. Antioxidant Activity:

The bioactive components of G. lucidum, like polysaccharides and triterpenes, have demonstrated very strong antioxidant properties. Such components neutralize the free radicals responsible for cellular damage through the induction of oxidative stress. Polysaccharides from G. lucidum have been proven to markedly inhibit ROS accumulation in cells with hydrogen peroxide-induced neuronal apoptosis [33].

3.5.2. Regulation of Antioxidant Enzymes:

G. lucidum has been observed to promote the induction of the endogenous antioxidant enzymes, such as SOD, catalase, and glutathione peroxidase. Such induction may help boost the body's natural resistance to oxidative stress.

3.5.3. Activation of Nrf2:

The Nrf2/Keap1 pathway is considered essential for the defence of a cell against oxidative stress. Some G. lucidum extracts were found to activate Nrf2, causing transcription of genes associated with antioxidant response. It would thus result in an enhancement of the capacity of the cell to fight against oxidative stress [34].

3.5.4. Neuroprotective Effects:

In neurodegenerative conditions, G. lucidum has been shown to be protective against oxidative stress- induced neuronal damage. Research studies have suggested that it inhibits apoptosis in neurons by regulating the expression of key proteins related to oxidative stress response, including Bcl-2 and caspases [33,35].

4. SYNERGISTIC EFFECTS WITH CONVENTIONAL THERAPIES

Ganoderma lucidum has received attention for synergy in combination with other types of cancer treatment, including chemotherapy and radiotherapy. This synergetic integration possibly improves the efficacy of the treatment while reducing side effects, which places G. lucidum as a helpful adjunct in the management of cancer.

4.1. Combination with chemotherapy and radiotherapy:

Studies show that Ganoderma lucidum can increase the efficacy of chemotherapy and radiotherapy. Clinical trials show enhanced therapeutic response when added to conventional therapy. A meta- analysis showed a relative risk of 1.50 (95% CI 0.90–2.51), implying patients who took G. lucidum had superior response rates compared to those on conventional treatment only. [36].

Such synergistic effects can be mediated through several biological pathways:

Induction of Apoptosis:

G. lucidum was found to induce apoptosis in cancer cells, which increases the cytotoxicity of chemotherapeutic agents. In vitro studies indicated that extracts of G. lucidum with chemotherapy drugs, such as Docetaxel and Flutamide, greatly increased the apoptosis rate and reduced cell migration in prostate cancer cell lines [37].

Immunomodulation:

G. lucidum enhances host immune functions in terms of increased percentages of CD3, CD4, and CD8 lymphocytes. This kind of immunomodulation can enhance the body's ability to fight cancer cells during conventional treatments.

Reduced Side Effects:

G. lucidum had reduced side effects such as nausea and insomnia compared to the patients on standard treatment only. It might, therefore, reduce the burden of the unpleasant symptoms experienced in the context of conventional cancer therapy [36].

4.2. Role as an adjuvant therapy:

As an adjunctive treatment, G. lucidum performs a significant function in enhancing outcomes for patients subjected to cancer therapies:

Quality of Life Improvement:

Research has also shown that treatment plans that incorporate G. lucidum treatments result in increased quality of life for patients than control groups when the treatment program is completed [36]. This is associated with both lower side effects of the treatment regimen and psychological impact of using natural supplements.

Long-term survival:

Although there are no adequate studies to make G. lucidum the first line in the treatment of cancer, it does show promise when used as an adjunct therapy as it does enhance the response of tumors and may eventually prolong survival. The supportive role of G. lucidum may be particularly useful for patients seeking complementary treatments in addition to conventional methods [36,38].

5. BENEFITS OF GANODERMA LUCIDUM IN CANCER TREATMENT

5.1. Immune boosting properties:

The most important benefit of Ganoderma lucidum is its ability to enhance immune function. Studies demonstrate that Ganoderma lucidum extracts stimulate immune responses, including the activation of natural killer cells and T lymphocytes, which are crucial in tumour immunity [24,36]. β-D-glucans have been characterized as one of the largest components within Ganoderma lucidum responsible for such immunomodulation. They stimulate the production of cytokines such as interleukin-1β and tumour necrosis factor-α, which are essential in activating immune cells and enhancing their antitumor activity [24,14].

5.2. Reduction of side effects from conventional cancer therapies:

Ganoderma lucidum has also been linked to reduced side effects, which are generally associated with conventional cancer therapies, including chemotherapy and radiation. It has been reported that patients who used Ganoderma lucidum during treatment had reduced fatigue and nausea levels compared to those who did not use it [36,14]. This is especially important since side effects often dictate the degree to which patients can adhere to treatment and improve their overall quality of life.

5.3. Quality of life improvements for patients:

Implication of Ganoderma lucidum in protocols for cancer treatments has been well associated with positive quality of life for patients. A pilot trial showed that using spore powder from Ganoderma lucidum enhanced all quality of life metrics for cancer patients, like emotional well-being and reduced level of cancer fatigue. This conclusion indicates that even though Ganoderma lucidum does have direct anticancer properties, there is also something positive about patients' experiences after being diagnosed and treated for this disease [39].

5.4. Potential for use in cancer prevention:

Recent evidence indicates that Ganoderma lucidum can also be responsible for cancer prevention. The contents in the mushroom include bioactive compounds such as triterpenes and polysaccharides, which have been indicated to exhibit anticancer properties through inhibition of tumour cell proliferation and metastasis [24,36]. More so, some these compounds induce apoptosis or programmed cell death in several cancer cell lines but not within normal cells. This selective action makes Ganoderma lucidum a promising candidate for further research into its preventive capabilities against different types of cancer [24].

6. CHALLENGES AND LIMITATIONS

6.1. Bioavailability issues:

Poor Absorption

The major problem with Ganoderma lucidum is its bioavailability. The active compounds, especially polysaccharides and triterpenes, are often poorly absorbed in the gastrointestinal tract. This poor bioavailability can drastically decrease the efficacy of Ganoderma lucidum as a therapeutic agent in cancer treatment.

Potential Solutions

To overcome such absorption challenges, researchers are discovering nanoparticle delivery systems. It can improve the solubility and stability of the active compounds, which will improve their absorption and therapeutic efficacy. For example, encapsulation of Ganoderma lucidum extracts within nanoparticles may result in better delivery to target tissues, maximizing the anticancer effect while minimizing adverse effects [36].

6.2. Standardization of extracts:

Variability in Preparation Methods

Another major drawback is the non-standardized method of preparation for Ganoderma lucidum extracts. Different extraction methods (solvents, such as water vs. alcohol; extraction time; and extraction temperature) lead to differences in the final product's potency and composition. Inconsistency is a major hurdle in clinical application and complicates comparison between different studies.

Impact on Potency

The variability can affect not only the efficacy but also the safety profile of Ganoderma lucidum products. Without standardized extraction protocols, it is difficult for healthcare providers to ensure that patients receive a consistent dose of active ingredients necessary for therapeutic effects [40,13].

6.3. Safety and toxicity concerns:

Evaluation of Long-Term Use

Ganoderma lucidum is generally considered safe and well-tolerated. However, concerns remain regarding long-term use, especially at high doses. Minor side effects have been reported, such as nausea and insomnia; however, there is a lack of comprehensive evaluations on long-term safety [36,41].

High-Dose Safety

High doses of this drug also need more research on their potential toxicity. While acute toxicity seems low according to the data available, chronic exposure to high doses could pose risks that have not been fully explored. Hence it is necessary to inform the patients of potential side effects and to monitor the health of the patients throughout treatment [37].

7. FUTURE PERSPECTIVES

7.1. Advancements in research on Ganoderma lucidum's bioactive compounds

Ganoderma lucidum (G. lucidum) has bioactive compounds, including polysaccharides, triterpenoids, sterols, proteins, nucleotides, fatty acids, vitamins, and minerals, which have an anticancer property such as immunomodulatory, anti-proliferative, cytotoxic, and antioxidant action. These metabolites have antioxidant, antitumor, and anti-inflammatory functions. Biochemical studies on G. lucidum revealed several categories of biologically active compounds that are responsible for health-promoting effects [42]. It was revealed by various studies that G. lucidum has pharmacological effects such as antioxidant, antitumor, anti-aging, anti-liver fibrosis, and immunomodulation [43].

7.2. Potential for personalized medicine and targeted therapies

The biological activities of G. lucidum are summarized into potential health benefits. G. lucidum has been administered to patients who suffer from various diseases, such as asthma, bronchitis, arthritis, hypertension, insomnia, diabetes, liver disease, nephritis, and cancer [42]. Active secondary metabolites in Ganoderma lucidum show good antioxidant activity that may open up avenues toward the development of drug leads [45]. Polysaccharides and peptides isolated from G. lucidum are used in traditional Chinese medicine for immunomodulatory purposes [46].

7.3. Exploring novel drug formulations and delivery systems

Clinical trials would be required to establish the promise of pharmaceutical preparations of G. lucidum, standardized with known active components, in cancer prevention and therapy. The different compositions of the G. lucidum products are attributed to the cultivation conditions, the process of extraction of the bio-compounds, and the origin or part of the fungus used. Many compounds from Ganoderma lucidum have demonstrated exemplary bioactive properties [44].

8. Conclusion

Ganoderma lucidum (Reishi) demonstrates anticancer activity in experiments on cancer cells and may be therapeutically valuable as a dietary supplement. Ganoderma lucidum may be used in hematological malignancies and can be introduced into the clinical setting [36]. However, higher-quality clinical studies are required to clarify the promise of medicinal mushrooms in cancer therapy

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