Exploring Ganoderma Lucidum Polysaccharides: A Potent Anti-Cancer Agent

Yanzhen Wang
Shanghai Starriver Bilingual School, Shanghai, 200000, China

Keywords: GLP, Cancer, Anticancer Effect.

Abstract: The article will focus on introducing Ganoderma lucidum, a mushroom that may be beneficial to humans. In the eyes of most people, Ganoderma lucidum is simply a traditional Chinese medicine with the function of calming people's mind and relieving the cough. In recent years, under the implementation of various experiments, however, scientists have gradually discovered the efficacy of Ganoderma lucidum in assisting in the treatment of cancer, so this fungus has quickly attracted people's attention. After extracting and analysing the internal substances of Ganoderma lucidum, scientists found that the Ganoderma lucidum polysaccharide (GLP) contained in it is one of the key components that enable Ganoderma lucidum to produce anti-cancer properties. In this article, some studies that are relevant to GLP are summarized, and the relevant experimental data collected from the internet are provided to demonstrate its pro-apoptotic and anti-proliferative effects on the cells.

1 INTRODUCTION

Ganoderma lucidum, which people commonly called Linzhi or Reishi, is a mushroom that has immerse health benefits in China, and is a traditional Chinese medicine that Chinese people often use it in their daily lives. As the famous Chinese herbal word says, "Ganoderma lucidum has a rich range of pharmacological components, including the components like polysaccharides, furans, alcohols, nucleosides, alkaloids, triterpenes, oils, various amino acids and proteins, enzymes, organic compounds, and various trace elements." This fungus was found to have the effect of helping the human body in ancient, and it has also attracted significant attention in recent years due to its reported anti-cancer properties, which scientists have just found out. After extracting and purifying the Ganoderma lucidum, scientists found that one of the key components that results in the anticancer effect of the Ganoderma lucidum is the Ganoderma lucidum polysaccharides, which is often called GLP. It exists in the fruiting bodies and the mycelium of the Ganoderma lucidum. After a series of experiments and operations, scientists prove that these components have significant anticancer potential effects to cancer cells through various mechanisms such as immunomodulation, anti-proliferation, pro-apoptosis, anti-metastasis, and anti-angiogenesis (Sohretoglu and Huang, 2018). In the early years, some scholars have proved that Ganoderma lucidum mycelium has a significant inhibitory effect on myofiber malignant tumors in mice, and also has an inhibitory effect on lung metastases. Intragastric administration of sarcoma mice could significantly inhibit the growth of sarcoma, and showed a dose-response relationship. Experiments have also been shown to significantly promote the expression of tumor necrosis factor in mouse macrophages, increase the production of TNF, and thus kill tumor cells. Ganoderma lucidum Fukangbao also has the effect of inhibiting tumor growth, and it has been found to have an inducing effect on interleukins in tumor-bearing mice, indicating that the drug exerts an inhibitory effect on tumors by regulating the host's biological response modulator system. Ganoderma lucidum decoction can significantly reduce the tumor weight and significantly reduce the activities of tumor marker enzymes glutamyl glycosyl-transferase and R-glutamphthalein transdermase in mice with ascites in charge of liver carcinoma, improve the killing power of macrophages to tumor cells, enhance the

Wang, Y.
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DOI: 10.5220/0013933000004914

In *Proceedings of the 2nd International Conference on Renewable Energy and Ecosystem (ICREE 2024)*, pages 303-307
ISBN: 978-989-758-776-4

proliferation of splenocytes, and thus inhibit tumor growth. The above studies have shown that a variety of preparations of Ganoderma lucidum have anti-tumor effects.

It is of vital importance to focus on the study of the function of GLP, as it has the ability to inhibit the proliferation of various cancer cells. As a new type of drug, Ganoderma lucidum has high research value, so the scientists increased their efforts on it, and they carried various of related experiments to study the efficiency. In this article, a series of experiments on studying the impact of GLP on the treatment of tumours are displayed, the relevant experimental data collected from the internet are also provided to demonstrate the Ganoderma lucidum ' s anti-proliferative and pro-apoptotic effects on the cells.

The experiments have demonstrated that GLP inhibits the growth of various of cancer cells in mice body, rats' adrenal medulla pheochromocytoma cells, human bladder cancer cells, and human colon cancer cells. As Ganoderma lucidum has shown significant inhibitory effects on the growth of various cancer cells, scientists generally believe that GLP has effects on the treatment of cancer, and they conducted several relevant experiments to further analyse the effect of GLP on the tumour cells. In this article, three typical articles are selected for analysis, and accurate conclusions are made based on the experimental data (Ma et al, 2023).

In addition to that, the anticancer effects of GLP can also be shown through various of pathways, including AKT and MAPK signalling pathway. These pathways all play crucial roles in mediating the effects of GLP. In the first example, how GLP affects the cancer cells is explained by modulating the eIF4e pathway and displaying the whole process, and it shows that GLP can effectively hinder tumour cell proliferation, promote apoptosis, and make it a valuable compound for exploring new cancer treatments.

In the experiment that use the human colon cancer cells, GLP has been shown to reduce cell viability in a concentration-dependent manner. Moreover, related to the experiment 2 in the article, GLP also induces apoptosis by preventing cancer' s mechanisms; GLP can enhance the release of lactate dehydrogenase (LDH), increase intracellular Ca2+ levels. These findings all emphasize the multifaceted ways that GLP can exerts its anticancer effects, providing a rich area for further investigation and therapeutic development.

In the example 3, the effects of Ganoderma lucidum polysaccharides on tumour growth is discussed by giving the experiment about using the cyclophosphamide-treated mouse cancer cells. In the experiment, scientists examined the alleviation of the cyclophosphamide induced immunodepression, and they also evaluated anti-metastatic effects of Ganoderma lucidum in cyclophosphamide -treated cells by giving and comparing specific experiment data. While the preliminary results are encouraging, before further research can consolidate its efficacy and safety, caution must be maintained when using the Ganoderma lucidum. Like any medicinal substance, Ganoderma lucidum may pose certain risks or interactions with existing treatments, though there are currently no relevant reports about the risk of using Ganoderma lucidum (Ge et al, 2023).

Moreover, the possibility of Ganoderma lucidum's effects being attributed to a placebo response cannot be dismissed. Placebo effects, driven by psychological factors, can sometimes lead to effective improvements in outcomes. Therefore, rigorous clinical trials are still necessary to differentiate between genuine therapeutic benefits and placebo effects associated with Ganoderma lucidum consumption. Although more researches are needed to fully understand the whole mechanism and potential drawbacks of Ganoderma lucidum, the field of natural medicine has broad prospects for future medical development. The continuous exploration has paved the way for innovative cancer therapies and new treatment methods.

In conclusion, while Ganoderma lucidum shows immense potential in the fight against cancer, comprehensive research efforts are indispensable to validate its efficacy, safety, and optimal usage. The development of medicinal fungal researches, especially those experiments about Ganoderma lucidum, allow us to glimpse the future where natural compounds plays a crucial role in the next generation of cancer treatment.

2 MECHANISM

GLP functions in various ways. It could activate and enhance the function of cytotoxic T cells that can directly attack the tumour to death; it promotes the activation of dendritic cells, hence initiating the immune responses against cancer and secreting antigens to T cells; it could stimulate B cell ' s activity, leading to increased production of antibodies that can target cancer cells; it can enhance the activity of the natural killer cells (NK), which play an important role in detecting and destroying cancer cells; it can help to enhance the macrophage function of the cells and increase cells' ability to engulf, and

finally eliminate the cancer cells. Through modulating these cells that have the immunity, Ganoderma lucidum polysaccharides can potentially enhance the overall immune response against cancer, helping the body's ability to effectively identify and destroy the cancer cells.

2.1 The Anti-Cancer Effects in Breast Cancer Cells

GLP reduces the expression of some signalling molecules, which may affect the spread of breast cancer in the body. Eukaryotic initiation factor 4E (eIF4E) can form eIF4F complexes with eIF4A and eIF4G to participate in the initiation of eukaryotic translation. Therefore, by binding to the cap structure at the 5 'end of mRNA, eIF4E can bring eIF4A to the 5' end of mRNA, allowing eIF4A to exert helicase activity to open the secondary structure at the 5 'end of mRNA. eIF4E is an oncogenic gene in various cancers, promoting cancer growth and proliferation. It may be a potential therapeutic target for cancer and a biological indicator for prognostic evaluation; The application of eIF4E inhibitors may provide a new approach for cancer chemotherapy. Phosphorylation can regulate the activity of eIF4E. For instance, phosphorylation of serine at position 209 of mammalian eIF4E can enhance the binding of eIF4E to capped mRNA and stabilize the interaction between eIF4E and eIF4G.] In the experiment, to examine whether Reishi treatment can affect the gene expression through pathways such as PI3K/AKT/mTOR, PI3K/AKT signal RT2 Profiler PCR array was used in SUM-149 cells. After treating them with the carrier and/or the 0.5mg/mL concentration Reishi solution provided in the experiment for about 3 hours, the experiment begins. Methods such as Real Time RT-PCR Analysis, Western Blot Analysis, Metabolic Labeling, Cap Binding Assay, Immunohistochemistry, and Statistical Analysis are being used during the process to get the data and to compare the results from these experiments (Rong, 2020).

Immunohistochemistry is a technique used to visualize the distribution of specific proteins or antigens in tissue samples. The method relies on the use of antibodies that bind to target proteins within cells or tissues, allowing them to be detected and localized. The binding of these antibodies to target proteins can be visualized under the special microscope, providing valuable information about the distribution of the protein within the sample, and the data can be collected. Immunohistochemistry is commonly used in research and diagnostic settings to study various diseases, understand cell function, and evaluate biomarker expression patterns in different tissues. It is a powerful tool for studying protein localization, identifying disease markers, and elucidating biological processes at the tissue level.

Ganoderma lucidum reduces the expression of these pathways' genes and mTORC1 effectors. The panel shows the gene expression effects by comparing data by dividing time into three parts. Down-regulated genes are on the left side of the row, while up-regulated genes are on the right side of the row. And the statistically significant genes are higher than the $P<0.05$ line. In panel B, the proteins are the same for each sample, with different lanes (tumour lysate from mice under vehicle or Ganoderma lucidum) showing different reflectance. Both of the panel show the effectiveness of the expression of the Ganoderma lucidum, which directly indicates that Ganoderma lucidum can help to reduce the signalling pathways during the process. Quantification was done, and the results showed that Ganoderma can significantly reduce the expression of key IBC proteins in vivo (Wei, 2021).

Tumours treated with Ganoderma in picture E above the text showed smaller size and lower Ki-67 and Vimentin levels compared to vehicle-treated mice, which may indicate reduced cell proliferation and stromal characteristics. These findings are consistent with the decrease in mTOR activity in Ganoderma-treated cancer cells. The study demonstrates that Reishi treatment in mice leads to significant reductions in tumour growth and weight. This effect is associated with decreased expression of key molecules in the signalling pathways mentioned above at both protein and gene levels, particularly affecting mTOR activity. Additionally, the research reveals concurrent downregulation of E-cadherin and p120-catenin along with reduced levels of eIF4G, supporting and expanding upon prior discoveries. In conclusion, the Ganoderma lucidum reduces tumour growth, weight, and it is also helpful to the proliferative of the marker expression. So, maybe, Ganoderma lucidum extract can be used as an anticancer therapeutic for the patients.

2.2 The Anti-Cancer Effects in Colon Cancer Cells

HCT-116 cell line is a test model to help to understand the hypothesis that GLP can influence the anticancer effects in this experiment. Researchers have found that GLP can reduce the cell viability of human colon cancer cells. As the concentration increases, the cell viability decreases. GLP induces

apoptosis by increasing the concentration of LDH and promoting Ca2+ levels in the cells, thereby activating JNK pathways. Ganoderma lucidum that is obtained from the basidiomycete fungal extracts has shown significantly inhibition on various kinds of cancer cells, including the colorectal cancer that this part mentioned. GLP, in vivo and in vitro, exerts the cytotoxic and anti-angiogenic to influence the tumour cells. Before the experiment, cells were treated with 5 mg/mL GLP for different time: 0h, 12h, 24h, 36h and 48 hours). After washing 3 times with PBS, cells were lysed in RIPA lysis buffer, and they were put on the ice for thirty minutes.

The study investigated the effect of GLP on HCT-116 cell viability, and it shows that GLP exhibits significant inhibitory effects on cell viability. The 50% inhibitory concentrations at 24h, 48h and 72 hours were 9.25, 5.72 and 3.69 mg/mL. The inhibitory activity of GLP lasts for at least 72 hours. Starch control experiments showed a dose-dependent decrease in cell growth, whereas 5 fluorouracil significantly inhibited cell viability. Significant changes have appeared in the cells that are treated with GLP, including the change of its shape, the decreasing of its volume, and the decreasing of the concentration-dependent cell numbers (Wang et al., 2018).

compared with the control group, a GLP solution with a concentration of 5 mg/mL significantly increased the activity of caspase-8. The results indicate that the activation of the caspase dependent apoptotic signalling pathway may involve the GLP induced apoptosis of human colon cancer cells. The presence of GLP provokes the activation of caspase-8 and enhances the expression of caspase-3, indicating that GLP induced cell death involves a caspase-dependent pathway. It also increased the abundance of Fas protein. By administering GLP treatment, the signal transduction of active caspase-8 was significantly increased, while the levels of Fas protein and caspase-3 were elevated.

In conclusion, this experiment introduces a new way on how GLP affects human colon cancer cells by stimulating cell death and promoting apoptosis. These results highlight the promising potential of GLP in colon cancer prevention and treatment, opening up avenues for further exploration in the field of pharmacology. The findings indicate that GLP could be a valuable candidate for developing new methods to combat colon cancer. The combination usage of Chinese herbal medicine and the radiotherapy can potentially inhibit various cancers, reduce treatment side effects, improve quality of life, and prolong the survival of cancer patients. Preliminary studies have shown that simultaneous treatment with GLP and 5-fluorouracil can inhibit in vitro cultured human colon cancer cells. Overall, experiments indicate that the antitumor properties of GLP are attributed to its subcomponents, particularly high molecular weight polysaccharides. The research explores how GLP affects human colon cancer cells by stimulating apoptosis through the ratio and triggering the mitochondrial intrinsic pathway, causing mitochondrial membrane depolarization (Lin, 2015).

2.3 Effects of the Ganoderma Lucidum that Is the Antlered Form on the Growth and the Metastasis on the Cyclophosphamide-Treated Mice Cancer Cells

In this experiment, the alleviating effect of the antlered shaped Ganoderma lucidum on immunosuppression induced by cyclophosphamide is examined, and the anti-tumour and anti-metastatic effects of Ganoderma lucidum AF in cyclophosphamide treated mice are examined. it shows that treatment with CY caused a decrease in the weight of C57BL/6 mice compared to the control group at the beginning of the experiment, but the weight began to increase starting from 4 days after the administration. However, if the diet that has 2.5% G. lucidum AF were given to the mice 7 days before CY administration, the weight loss induced by CY was inhibited by G. lucidum AF, so in most of days, the weight of the mice that use Reishi and CY is bigger than the weight of mice that only use CY. C57BL/6 mice were fed either a standard diet or a diet containing 2.5% GLP AF solution for a week, followed by an injection of 150 mg/kg of CY. Data were collected at days 3, 5, and 7 post-injection. NK cells activity was measured at the effector-target ratios of 40:1 and 80:1. The results showed that NK activity changed over time after CY administration. Statistical differences between groups ($p < 0.05$) were observed using ANOVA and Fisher's PLSD post hoc test. Data demonstrate the potential impact of dietary factors on NK cell function after CY treatment in this mouse model (Lin et al., 2004). In these three groups, the sample with the adding of CY and Reishi shows the highest splenic NK activity rate, which also indicates the efficiency of Reishi. Hence, from analysing the data given above, we can get the conclusion that the use of G. lucidum AF can improve the effectiveness of cancer treatment by preserving natural killer cell activity (Unlu et al., 2016 & Ahmad, 2020).

3 CONCLUSION

Previous studies have suggested that compounds found in Ganoderma lucidum may have anti-tumour properties by inhibiting the angiogenesis, which is the process by which tumours form new blood vessels to sustain the cancer cells' growth. By disrupting this process, Ganoderma lucidum can slow down or even prevent the spreading speed of cancer cells to other parts of the body. Additionally, some studies suggest that Ganoderma extract may have immunomodulatory effects, enhancing the body's immune response against cancer cells.

From my personal perspective, Ganoderma lucidum really has great potential in cancer treatment. It can be found in the natural world, and it has a relatively low toxicity compared to nowadays other medicines. Both of these traits make the Ganoderma lucidum as an attractive field for the further research. Integrating Ganoderma lucidum into medical practice could provide patients with a complementary approach to managing cancer-related symptoms and potentially improve treatment outcomes.

Although Ganoderma has shown potential as an adjunct to cancer treatment, more comprehensive clinical trials are needed to fully understand its efficacy and safety. It will be important for scientists to conduct further research to determine the optimal method to use the Ganoderma lucidum. Only through rigorous testing can the medical community effectively incorporate Ganoderma into mainstream cancer treatments.

In conclusion, while Ganoderma lucidum may not be a standalone cure for cancer, its ability to inhibit tumour growth and modulate immune responses positions it as a valuable tool in the fight against cancer. Continued research and clinical trials will be essential in unlocking the full therapeutic potential of Ganoderma lucidum and integrating it into mainstream oncology practices. Ultimately, the future looks bright for Ganoderma lucidum as a complementary therapy in cancer care, offering hope for improved patient outcomes and quality of life.

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