In Vitro and in vivo Studies of *Ganoderma lucidum* in Cancer

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Abstract

Current cancer therapy such as chemotherapy and radiography are known to possess many side effects that could lead to serious complications. The application of natural product as complementary and alternative treatment provides significant advantages. It could increase the sensitivity of chemotherapy and radiography while at the same time reducing their associated side effects and complications. With regards to anticancer drugs, more than 50% of the modern oncological drugs are derived from natural products. An edible mushroom, *Ganoderma lucidum* has long been used in traditional and conventional medicine in China, for the prevention and treatment of various human diseases.

The fungus possesses a wide variety of bioactive compounds present in its fruiting bodies, mycelium and spores, including anticancer property that has been proven in vitro and in vivo studies. The carcinostatic effects of *G. lucidum* have been shown in a variety of cancer cell lines, including breast, pancreas, lung, colon, skin and prostate. This paper presents in vitro and in vivo studies of the anticancer properties of *G. lucidum* in cancers.

Keywords: *Ganoderma lucidum*, cancer, medicinal herbs, alternative medicine.


Received date: 07 May 2019  
Accept date: 20 August 2019

Introduction

From thousands of years ago, medicinal herbs have long been used as a natural remedy by the ancient people. Even in this 21st century, medicinal plants still continue to play a central role in the healthcare system of the world’s population. Currently, western medicine has started accepting natural products from Traditional Chinese Medicine. There is also an increasing popularity of herbal therapies for the treatment of cancer in the United States. Most of the commercially available mushrooms contain free radical scavenging, reducing power, chelating effects on metal ions, and antioxidant properties. Among these mushrooms, *G. lucidum* has long been used in traditional and conventional Chinese medicine for the prevention and treatment of various human diseases.

Contemporary research indicates that *G. lucidum* and some other species of the *Ganoderma* genus contain bioactive constituents, including polysaccharides like beta-glucans and triterpenes like gandoric acids. Hence, scientific justification based on the elucidation of mechanisms responsible for the biological effects of these natural products could help validate their use in alternative or adjuvant cancer therapies.

The primary reason for using this type of plant-based medicine is because it could reduce the side effects and complications associated with chemotherapy and radiotherapy. Currently, the major standard cancer therapies widely used are still surgery, chemotherapy, and radiotherapy. Although chemotherapy and radiotherapy are effective against cancer, they also possessed serious side effects and complications such as fatigue, pain, diarrhea, nausea, vomiting, and hair loss. The clinical use of the chemotherapy drug is limited due to cellular resistance and dose-dependent toxicity in normal tissue. Hence, the use of natural...
products as complementary and alternative medicine could be applied to treat cancer, as it has significant advantages in terms of increasing the sensitivity of chemotherapy and radiotherapy, as well as reducing their associated side effects and complications.\(^{11}\)

**Ganoderma lucidum and Its Major Bioactive Compound**

Ganoderma lucidum (G. lucidum) belongs to the family of Ganodermataceae (Basidomycetes), which is a type of an edible mushroom used in complementary and alternative medicine particularly in Asian countries.\(^{12}\) This mushroom is used traditionally for treating many kinds of diseases, including cancer.\(^{13}\) Ganoderma lucidum exerts a wide variety of pharmacological properties, such as antioxidant, antitumor, anti-inflammatory, antinociceptive, hypertension, bronchitis, arthritis, chronic hepatitis, gastric ulcer, hypercholesterolemia, immunological disorders, and scleroderma.\(^{14}\)

There are over 300 bioactive compounds from the fruiting body, spores and mycelia of G. lucidum that have been isolated or detected.\(^{15}\) The main known bioactive molecules from G. lucidum are triterpenoids, polysaccharides, nucleotides, fatty acids, glycoproteins, sterols, steroids, proteins or peptides and trace elements.\(^{16}\) Among these bioactive molecules, the two main groups which have been identified to exhibit anti-cancer effects are triterpenoids and polysaccharides.\(^{17}\)

In general, the basic chemical structure of triterpenoids in G. lucidum is that of an oxygenated lanostane.\(^{18}\) Lanostane-type triterpenoids in G. lucidum can be divided into about ten groups depending on structural similarities and functional groups.\(^{15}\) These includes ganoderic acid (GA), ganosporeric acid, methyl ganoderate, ganodspore lactone, ganoderenic acid, ganolucidic acid, methyl ganolucidade, ganoderiol, ganoderal, epoxyganoderiol, methyl lucidenate, lucidone, ganolactone, lucidumol, lucialde-hyde and so on.\(^{19}\) At least 50 triterpenoids are unique to G. lucidum. The first triterpenoids isolated from G. lucidum are GA-A and GA-B in 1982.\(^{19}\) Structure-activity relationship assays of 43 triterpenoids separated from G. lucidum revealed that the type of side-chain, C-3 carbonyl group, double bonds (D7,8, D9,11), and number of hydroxyl groups are important in the cytotoxicity of G. lucidum triterpenoids.\(^{15}\)

The major component of polysaccharides in G. lucidum is glucose, where it was indicated from the structural analyses of G. lucidum polysaccharides (GL-PS).\(^{20}\) However, GL-PS can also contain xylose, mannose, galactose, and fucose in different conformations as it is heteropolymers.\(^{21}\) Besides that, the anti-tumorigenic properties of these polysaccharides are affected by branching conformation and solubility characteristics.\(^{22}\)

The function of polysaccharides of G. lucidum mainly acts as immunomodulators or antioxidants in vivo to resist cancer, while triterpenoids, mainly function to inhibit cancer cell proliferation and metastasis.\(^{23,24}\) The proportions of triterpenoids and polysaccharides in G. lucidum are not fixed in G. lucidum.\(^{25}\) This may be due to variations in species, cultivation, growing area and extraction method of G. lucidum.\(^{15}\) Even in the same mushroom, the composition of triterpenoids and polysaccharides varies greatly from the fruiting body, spore and mycelia of G. lucidum.\(^{15}\)

**Ganoderma lucidum Treatment in Cancer**

Progression of cancer involves a series of multiple processes of abnormal genetic and epigenetic events which leads to malignant transformation.\(^{26,27}\) G. lucidum demonstrates an anti-cancer activity in an in vivo and in vitro studies.\(^{28}\) Various types of solvent have been used to extract the bioactive compound of G. lucidum and these extracts have shown to have caracostatic effects in a wide variety of cancer cell lines, including breast, pancreas, lung, colon, skin, and prostate.\(^{28}\)

G. lucidum also contributes to anticancer activity by inhibiting the signalling pathways involved with cell adhesion, proliferation, survival, invasion, and degradation of the extracellular matrix.\(^{13}\) Several studies had conducted on the effects of G. lucidum towards cancer cell are tabulated in Table 1.

A previous study done by Dai et al. (2014) reported that both CX43 and VEGF play an important role in the genesis and development of ovarian cancer.\(^{29}\) It was demonstrated that G. lucidum inhibits ovarian cancer by down-regulating the expression of VEGF and up-regulating the downstream Cx43 expression.\(^{29}\)
using the human ovarian cancer cell line (HO 8910).

The study suggested that several biologically active pathways, including the apoptotic pathway were identified to be associated with GWh anticancer activities. Thus, this shows the potential anticancer effects of G. lucidum, including the inhibition of cell cycle, induction of apoptosis, and the reduction of tumour progression.

Loganathan et al. (2015) reported that G. lucidum extract suppressed the expression of genes involved in the invasive behaviour of human breast cancer cells (MDA-MB-231) cell line. In addition, it was also reported that G. lucidum extracts inhibit breast-to-lung cancer metastasis of the highly invasive human breast cancer cells implanted in mouse mammary tissue.

An in vivo study done by Deepalakshmi et al. (2013) using Sprague Dawley rats reported that G. lucidum ethanolic extract exhibited potent anti-oxidant effects and could enhance enzymatic antioxidants like superoxide dismutase, catalase, and glutathione peroxidase in rat mammary carcinogenesis.

A preliminary study was done by Syairah et al. (2017) to determine the effects of G. lucidum extract towards oral cancer cell (ORL-48T). The study reported that G. lucidum extract decreased cell viability significantly in a concentration related manner, which reflects the cytotoxic effect of G. lucidum towards ORL-48T. Hence, there are many mechanisms by which the G. lucidum extracts exhibit anti-cancer activities, including the direct inhibition of cell viability, inhibition of cell proliferation through cancer-specific cell cycle arrest and apoptosis. Besides, several studies have shown that the treatment of cancer cells with G. lucidum extracts can lead to down-regulation of cell cycle-associated proteins resulting in cell cycle arrest in cancer cells.

Conclusions

In conclusion, the application of an alternative treatment in cancer treatment using natural products is crucial as it could increase the sensitivity of chemotherapy and radiotherapy, as well as reduce their associated side effects and complications. The use of traditional Chinese medicinal mushroom, G. lucidum as an alternative cancer treatment could be employed.
This is because *G. lucidum* has been shown to have anti-cancer activity in the in vitro studies and cytotoxic effects in the in vitro studies, including breast, prostate, ovary, colon, and liver cancers. However, a thorough research regarding the effects of *G. lucidum* on human cancer is essential before the development of *G. lucidum* as an alternative medicine could be established.

**Acknowledgments**

The authors wish to acknowledge the Fundamental Research Grant Scheme (600-rmi/FRGS5/3(25/2015), provided by the Ministry of Education Malaysia and initative Research Grant (600 IRMI/MyRa 5/3/GIP (050/2017) by Universiti Teknologi MARA, Sungai Buloh campus, Selangor, Malaysia.

**Declaration of Interest**

The authors declare that there is no conflict of interests regarding the publication of this paper.

**References**


