Effect of *Ganoderma lucidum* (*G. lucidum*) on the Liver of Mice Bearing Ehrlich Solid Tumor (EST) and Exposed to γ-Radiation.

*Ibrahim, S.I. * and El-Kabany, H. **

Radiation Biology* and Health Radiation Research ** Dept., National Centre for Radiation Research and Technology, Nasr City, Egypt

E-mail: hananelkabany@yahoo.com

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**ABSTRACT**

The present study was performed to investigate the antitumor and radio sensitizing efficacy of *Ganoderma lucidum* (*G. lucidum*) and to evaluate its potential to improve hepatic dysfunction in Ehrlich solid tumor (EST) bearing mice. *G. lucidum* (100mg/Kg body weight) was administered orally to EST bearing mice for 15 days before and 15 days after tumor inoculation. Irradiation was carried out the 8th day of tumor inoculation when the diameter of the tumor reached approximately 10mm. Mice were exposed to fractionated doses of whole body γ-radiation (3x2Gy) at two days interval to attain a total dose of 6 Gy. Mice were divided into 6 groups (15 mice in each group) as follows: normal control, mice treated with *G. lucidum* for 30 days, EST bearing mice, EST bearing mice exposed to fractionated doses of γ–radiation (2Gy x 3), EST bearing mice treated with *G. lucidum* for 15 days before and 15 days after tumor inoculation and EST bearing mice received combined treatment radiation and *G. lucidum*. Five mice from each group were sacrificed, after 18hr fasting after the last dose of *G. lucidum* treatment. Blood was collected, liver and tumor were removed for biochemical and histopathological studies. The remaining animals were observed for recording survival percentage and tumor size. In *vitro* study on Ehrlich Ascites Carcinoma cells showed that the percentage of nonviable cells (NVC%) increase with increasing *G. lucidum* concentration. The results revealed also that treatment of EST bearing mice with *G. lucidum* and/or γ-radiation increased the survivability and decrease the tumor size as compared to EST group. The biochemical analysis for EST bearing group recorded an elevation in the activities of lactate dehydrogenase (LDH), asparta amino transferase (AST) and alanine amino transferase (ALT) in the serum. Also, there
was an elevation in the concentration of malondialdehyde (MDA), a marker of lipid peroxidation, accompanied by a decrease in superoxide dismutase (SOD) activity and glutathione (GSH) content in liver tissues. A remarkable increase was observed in alpha-fetoprotein (AFP) and interleukin-2 (IL-2) concentration in serum as compared to normal control. Liver of tumor bearing mice showed focal tubular necrosis associated with inflammatory cells infiltration, and vacuolation of the hepatic cells. Furthermore, an elevation of tail DNA % was recorded in the tumor tissue of mice treated with G. lucidum and/or γ-irradiation compared to EST control group. Treatment of EST bearing mice with G. lucidum and/or irradiation ameliorated the change in biochemical parameters and improved the histopathological changes in EST bearing mice. It could be concluded that G. lucidum might have anti-tumor properties and a radio protective role in normal tissues as well as a radio sensitizing effect in tumor tissues.

**Keywords:** Ganoderma lucidum, Ehrlich Solid tumor, γ-rays, liver, antioxidant status.

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**INTRODUCTION**

Cancer constitutes the largest cause of mortality in the world and claims over 6 million lives every year (1). It is a disease in which cellular growth regulatory networks are disrupted (2). An extremely promising strategy for cancer prevention today is chemoprevention, which is defined as the use of synthetic or natural agents alone or in combination to block the development of cancer in humans (3). Solid tumors often contain hypoxia and necrosis regions where the cells are prone to acquire resistance to conventional treatment, such as radiotherapy and chemotherapy (4).

A benefit of ionizing radiation as a therapeutic tool is the possibility to apply it loco regionally thereby preventing systemic toxicity. However, like chemotherapeutic agents ionizing radiation, which can lead to severe side effects in the surrounding tissue after the therapy. In addition there are large numbers of human malignant tumor cells that respond poorly to ionizing radiation. However, radiation dose to the tumor cannot be increased as needed because of the normal tissue toxicity in the radiation field. Hence there is a need for chemical agents which upon contact with tumor cells increase their sensitivity to radiation thus minimizing large doses of radiation and also spare normal tissue from combined toxic effects (5).
Radiosensitizers, like radioprotectors, have also been defined differently by researchers. Urtasun (1998) defined radiosensitizers as compounds that when combined with radiation will achieve greater tumor inactivation than would have been expected from the additive effect of each modality. While Bump et al. (2003) defined radiosensitizers as agents that don’t have a therapeutic effect of their own but act to enhance the therapeutic effect of radiation. The synthetic radioprotectors and radiosensitizers currently available are toxic at their effective doses, and consequently natural product, particularly herbs are receiving attention. Herbal have been reported to act radiosensitizers under in vitro and in vivo conditions.

Fungi are an attractive source of physiologically functional foods and drug precursors, displaying a wide range of pharmacological activities such as anticancer, anti-inflammatory, antitumor and immune modulating effects.

Of approximately 10,000 known species of mushrooms, 2000 are safe for people health and about 300 of them possess medicinal properties. G. lucidum, a fungus grown on rotten wood, is a well known source of therapeutic agents. It is commonly known as Reshi or Lingzhi, and has been extensively used in oriental folk medicine for thousands of years to treat various diseases including cancer. The fungi G. lucidum has been used for long time in China to prevent and treat various human diseases such as bronchitis, hepatitis, hypertension, tumorgenic diseases, and immunological disorders.

Modern pharmacological and clinical investigations demonstrated that G. lucidum had anti-tumor and immunomodulatory activities. Its anti-tumor and immunomodulatory properties, along with low cytotoxicity, raise the possibility that it could be effective in the cancer patients receiving conventional chemotherapy and/or radiation treatment, to build up immune resistance and decrease toxicity. A number of reports have demonstrated that G. lucidum polysaccharides stimulated immune function both in vivo and in vitro, and the anti-tumor effect of G. lucidum was supposed to be the results of its immune-related mechanism or possible direct cytotoxic activity mechanisms.

Joseph et al. (2011) investigated that G. lucidum possessed significant antioxidant, anti-inflammatory, anti-hypertensive, anti-histaminic, anti-tumour, and anti-hepatotoxic effects. Large numbers of studies have shown that G. lucidum modulate many components of the immune system such as the antigen-presenting cells, NK cells, T and B lymphocytes. The water extract and the polysaccharides fraction of G. lucidum exhibited significant anti-
tumor effect in several tumor-bearing animals mainly through its immune enhancing activity\(^{(18)}\).

The aim of this work was to investigate the antitumor and the radio sensitizing efficacy of *G. lucidum* and to explore its potential to improve hepatic dysfunction in Ehrlich solid tumor bearing mice.

**MATERIALS AND METHODS**

**Experimental animals:**

Adult female Swiss albino mice (22-25g) obtained from the breeding unit of the Egyptian Organization for Biological Products and Vaccines, Cairo, were used in this study. The animals were maintained on a commercial standard pellet diet and water *ad libitum*.

**Radiation process:**

Whole body γ-irradiation was performed using a Canadian gamma cell-40 \(^{\text{137}}\)Cs at the NCRRT, Cairo, Egypt. Mice were exposed to fractionated doses of whole body γ-radiation (3x2Gy) at two days interval to attain total accumulative dose of 6 Gy after 8 days of tumor inoculation, when the diameter of the tumor reached approximately (10mm).

**G. lucidum preparation:**

*G. lucidum* obtained from DXN marketing company Malaysia was dissolved in distilled water. The mice were administered orally the proper dose of *G. lucidum* (100mg/Kg b.wt.) for one month according to Kwon and Kim (2011)\(^{(21)}\). In the present study, *G. lucidum* (100mg/Kg body weight) was administered orally to EST bearing mice for 15 days before and 15 days after tumor inoculation.

**In vitro cytotoxicity study:**

Short-term cytotoxicity of *G. lucidum* was assessed by incubating 2.5 \(\times\) 10\(^5\) EAC cells in 1 ml saline with varying concentrations (25-100µg/ml) of the *G. lucidum* at 37 C˚ for 2 hr. The viability of the cells was determined by trypan blue exclusion method described by El-merzabani *et al.*(1979)\(^{(22)}\).

**Tumour transplantation:**

A cell line of Ehrlich Ascites Carcinoma (EAC) was used in this study. The parent line was supplied from Egyptian National Cancer Institute (NCI), Cairo University. The tumor line was maintained in the experimental female
Swiss albino mice by weekly intraperitoneal injection of 2.5 millions cells per mouse. The EAC cells were counted before intraperitoneal injection using the bright line haemocytometer and dilution was done using physiological sterile saline solution. The desired numbers of cells were injected in a volume of 0.2 ml. To induce Ehrlich Solid Tumor (EST), 0.2 ml EAC cells (2.5x 10^6 cells /mouse) were inoculated intramuscularly in the right thigh of the lower limb of female mouse.

**Experimental design:**

90 female Swiss albino mice were divided randomly into 6 groups (15 mice in each group). First group: normal mice (control); second group: mice treated with *G. lucidum* (G.L); third group: mice bearing Ehrlich solid tumor (EST); fourth group: EST bearing mice exposed to γ-radiation (EST+IRR); fifth group: EST bearing mice treated with *G. lucidum* (EST+G.L); sixth group: EST bearing mice treated with *G. lucidum* and exposed to γ-radiation (EST+IRR+G.L).

**Tumor volume monitoring:**

The change in tumor volume was measured regularly twice weekly using Vernier calipers and calculated by the following formula according to Osman et al., 1993 (23).

\[
\text{Tumor volume (mm}^3) = 4\pi\left(\frac{A}{2}\right)^2 \cdot \left(\frac{B}{2}\right)^3
\]

Where A is the major axis and B is the minor axis.

**In vivo study:**

Five mice from each group were sacrificed, after 18 hr fasting after the last dose of *G. lucidum* administration (30 days from the beginning of the experiment period). Blood samples were collected by heart puncture and centrifuged to separate serum for biochemical studies. The liver was removed and divided in two parts. A known weight was homogenized with distilled water to obtain 10% homogenate for biochemical analysis and the other part was kept in 10% formalin for histopathological studies. Also, tumors were removed for comet assay. The remaining animals were observed for recording survival percentage and tumor size.

**Biochemical analysis:**

The activity of aspartate aminotransferase (AST) and alanine
aminotransferase (ALT) in serum was determined by a colorimetric method as described by Reitman and Frankel (1957) (24), LDH was assayed according to Bais and Philcox (1994) (25). Estimation of plasma alpha-fetoprotein (AFP) was carried out by enzymatic linked immunoassay (Elisa technique) using commercially available kit supplied by CALBIOTECH, INC. Interleukin-2 (IL-2) was estimated using enzyme-linked immunosorbent assay for the quantitative detection, using bender medical systems kits by Campus Vienna Biocenter 2 (Vienna, Austria, Europe). The comet assay carried out was based on the method of Singh et al. (1988) (26). Lipid peroxidation content was determined by measuring the malondialdehyde (MDA) end product in tissue according to the method of Yoshioka et al. (1979) (27). Superoxide dismutase (SOD) activity was estimated by the detection of superoxide anion using nitro blue tetra zolium formazan colour development according to Minami and Yoshikawa (1979) (21) and reduced glutathione content (GSH) was estimated as yellow colour which developed when 5,5 dithiol-bis (2-benzoic acid) is added to sulphydryl compounds according to Beutler et al., (1964) (29).

**Histopathological examination**

At the time of sacrifice, section of the liver was excised from mice. Samples were fixed in 10% formalin and embedded in paraffin and stained with hematoxylin and eosin according to method adopted by Drury and Wallington (1980) (30) and examined by light microscope.

**Statistical analyses**

All data were expressed as mean ±SE (standard error). Data were assessed by using a one-way ANOVA using SPSS 15.0 program and values of p < 0.05 was considered statistically significant.

**RESULTS**

The tumourcidal effect of *G. lucidum* at different concentration on the viability of Ehrlich ascites carcinoma cells expressed as percentages of non viable cells (NVC%) to the total cells as shown in table (1). The effect of *G. lucidum* on Ehrlich ascites carcinoma viable cells was in a dose dependent manner, since the % NVC increase with increasing the concentration of *G. lucidum*. The %NVC showed 30%, 50%, 80%, 100%, and 100% at concentration 10, 25, 50, 75, and 100 µg/ml respectively.
Table (1): In vitro antitumor activity of G. lucidum:

<table>
<thead>
<tr>
<th>Conc. of G. lucidum (µg/ml)</th>
<th>10</th>
<th>25</th>
<th>50</th>
<th>75</th>
<th>100</th>
</tr>
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<tbody>
<tr>
<td>%NVC</td>
<td>30%</td>
<td>50%</td>
<td>80%</td>
<td>100%</td>
<td>100%</td>
</tr>
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%NVC = C/T x 100
C: Number of non viable cell
T: Total number of cell

Survival and body weight:

As shown in Fig. (1), 90% of normal mice and 80% of mice given G. lucidum survived to the end of experiment. On the other hand, intramuscular inoculation of mice with EAC cells without receiving any further treatment caused the death of all the animals within 23 days post inoculation. Either exposure of mice to γ-rays or treatment with G. lucidum resulted in 30% animal survival 40 days after tumor inoculation. While 40% of mice in the group treated with G. lucidum and exposed to γ- radiation survived 40 days post tumor inoculation. Tumor size of EST control showed a progressive increase with time, while a remarkable delay in tumor size was observed in EST mice treated G.L and/or exposed to γ-irradiation as shown in Fig. (2).

![Fig.(1) Survival percentage of different groups.](image1)

![Fig. (2): Tumor size of EST bearing mice groups.](image2)
**Serum level of ALT, AST and LDH activities of different mice group:**

Hepatic enzymes AST, ALT and LDH of normal mice treated with *G. lucidum* were similar to normal mice indicating that *G. lucidum* has no toxicity. On the other hand, there was a marked elevation in serum activities of AST, ALT and LDH, in untreated EST bearing mice, comparing with corresponding control group. An elevation in the activity of ALT was observed in Ehrlich solid tumor bearing mice exposed to γ-irradiation. While, treatment of EST bearing mice with *G. lucidum* either alone or in combination with γ-irradiation showed a significant decrease in hepatic enzymes, compared to EST control. The combined treatment of *G. lucidum* and exposure to radiation and EST bearing mice resulted in non significant change in AST level compared to healthy control as shown in Fig. (3).

![Graph](image)

**Fig. (3):** Serum ALT, AST and LDH activities of different mice groups.

Each value represents mean± SE (n=5) significant value at p< 0.005

a: Significant against control group.  
b: Significant against EST group.
**MDA level, SOD activity and GSH content in liver tissue of different mice groups:**

The result obtained in the present study showed that either EST bearing mice or those exposed to γ-radiation resulted in a marked elevation in MDA concentration in liver tissue, accompanied by marked decline of SOD activity and GSH content, compared to normal control (Fig.4). In the group of EST bearing mice treated with *G. lucidum*, a remarkable improvement in MDA level and SOD activity, while a non significant increase in GSH content were observed. Combined treatment of *G. lucidum* and γ–radiation resulted in a significant decline in MDA level in liver tissue accompanied by a significant elevation in SOD activity and GSH content, compared to EST group, and a non significant change in MDA content was observed in the EST bearing mice group treated with *G. lucidum* as compared to normal control, as shown in Fig. (4).

Fig. (4): MDA level, GSH content and SOD activity in liver tissue of different mice groups.

Legends as in Fig. (3)
**Effect of *G. lucidum* on some tumor markers levels:**

Fig. (5) shows that, the AFP and IL-2 in serum of EST bearing mice showed significant increase compared with normal control. After administration of *G. lucidum* to EST bearing mice groups and/or exposure to γ-radiation, the level of AFP and IL-2 were significantly reduced as compared to the EST group.

![Graph showing levels of AFP and IL-2](image)

**Fig. (5): Levels of AFP and IL-2 in serum of different mice groups.**

Legends as in fig. (3)

**Comet assay of tumor tissue:**

The comet assay used here has the advantage of allowing observation of DNA strand breaks induced by genotoxic agents or γ-irradiation in isolated tumor cells. The results revealed an elevation of tail DNA % in mice treated with *G. lucidum* or γ-irradiated groups as...
compared to EST control group. Meanwhile, average background DNA damage in tumor was significantly higher in the EST bearing mice treated with G. lucidum combined with IRR group compared with EST control (Fig.6-a,b,c,d).

<table>
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<tr>
<th>a) EST control</th>
<th>b) EST+IRR</th>
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<tr>
<th>c) EST+G.L</th>
<th>d) EST+IRR+G.L</th>
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Fig. (6): DNA% damage in tumor cell tissues.

**Histopathological studies:**

Administration of G. lucidum to mice showed little sinusoidal dilatation. However normal appearance of the majority of hepatocytes was still observed (Fig.7a). Liver of tumor bearing mice showed focal tubular necrosis associated with inflammatory cells infiltration, and vacuolation of the hepatic cells (Fig.7b). In solid tumor bearing mice treated with G. lucidum, the liver tissue showed dilatation and congestion of hepatic sinusoids with individual cell necrosis and hypertrophied kupffer cells (Fig.7c). On the other hand, cytoplasmic vacuolization of hepatocytes and focal hepatic necrosis associated with inflammatory cells infiltration were observed in the liver tissue of solid tumor bearing mice exposed to γ-radiation. (Fig.7d). Sections of liver tissue of solid tumor bearing mice treated with G. lucidum and exposed to γ-radiation showed cytoplasmic vacuolization of hepatocytes (Fig.7.e).
Fig. (7): Photomicrographs of liver sections of mice under studies a: normal mice treated with *G. lucidum* b: EST control c: EST bearing mice exposed to γ-irradiation d: EST bearing mice treated with *G. lucidum* e: EST bearing mice treated with *G. lucidum* and exposed to γ- radiation (H&E X-400).

**DISCUSSION**

*G. lucidum* is traditionally used for the prevention and treatment of a
large number of diseases, including many forms of cancer \( ^{(20)} \). Earlier studies reported antitumor, antioxidant, anti-inflammatory and antinociceptive inhibited activities exhibited by crude extracts of southern Indian accessions of \( G. \) \( lucidum \)\(^{(31-32)} \).

The biological activities of polysaccharides or polysaccharide-protein complexes derived from mushrooms have received much attention in biomedical science. One of the most promising activities of these polysaccharides is their immunomodulating and anti-cancer effects \(^{(33)} \). It is widely accepted that antitumor polysaccharides from higher fungi enhance various immune responses modifiers \(^{(34)} \).

In the present work in vitro study showed that the effect of \( G. \) \( lucidum \) on Ehrlich solid tumor cells was dose dependent since the non viable cells increase with increasing \( G. \) \( lucidum \) concentration. Also, treatment of EST mice with \( G. \) \( lucidum \) and/or exposure to \( \gamma \)-radiation resulted in a remarkable improvement in survival percentage and a decrease in tumor size compared to EST control. Also, Joseph et al. \((2011)\) \(^{(20)} \) found that, administration of \( G. \) \( lucidum \) prior to tumor inoculation inhibited tumor volume and tumor size.

The results obtained in this study showed that Ehrlich solid tumor induced elevation in serum AST, ALT and LDH activities. The increase is in agreement with previous findings \(^{(35)} \). LDH is the consequence of the dissipation of the cell membrane of a large fraction of dividing malignant cells whose metabolic hallmark is anaerobic glycolysis that leads to increased LDH enzyme activity \(^{(36)} \). The increase in serum liver enzymes activity by the tumor may be due to the damage of cellular membranes of hepatocytes, which in turn leads to an increase in the permeability of cell membranes and facilitates the passage of cytoplasmic enzymes outside the cells leading to the increase in the serum enzymes activity. Treatment of EST bearing mice with \( G. \) \( lucidum \) and/or \( \gamma \)-irradiation diminished significantly the increase in AST, ALT and LDH in treated mice indicating the protective effect of this compound on the liver tissues. In previous studies, Joseph et al., \((2011)\) \(^{(20)} \) found that, \( G. \) \( lucidum \) polysaccharides induce apoptosis, inhibit cell proliferation and suppress cell migration of highly invasive human prostate cancer cells. The mechanism of antitumor activity of \( G. \) \( lucidum \) polysaccharides proceeded through stimulation of host defense responses \(^{(37, 38)} \). It was reported that, both the lipids extracted from the germinating spores and the sporoderm-broken spores of \( G. \) \( lucidum \) had remarkable anti-tumor effects, and could significantly inhibit mouse...
hepatoma, sarcoma with an inhibition of 80 % -90 % \((39)\).

The exposure to ionizing radiation is known to induce oxidative stress through generation of ROS resulting in imbalance of the pro-oxidant and antioxidant activities ultimately resulting in cell death \((40)\). A major biomarker of oxidative damage to living cells is increased lipid peroxidation.

A number of mechanisms are involved in radiosensitization, some of the commonly reported mechanisms include: 1) enhanced generation of ROS & RNS2) selective depletion of tumor cell antioxidants and antioxidant enzymes 3) increased lipid peroxidation, depletion of glutathione 4) elevated levels of lipid peroxidation and DNA damage of tumor cells 5) formation of DNA adducts6) inhibition of DNA repair 7) inhibition of DNA synthesis 8) induction of cell cycle arrest 9) induction of apoptosis10) depletion of protein kinase C \((8)\).

In the present study, MDA, which is a good indicator of lipid peroxidation\(^{(41)}\) increased in the liver of whole body \(\gamma\)-irradiated mice, indicating oxidative damage. \textit{G. lucidum} significantly reduced the elevated levels of lipid peroxidation in EST-treated mice. This might be attributed to the antioxidant and free radical quenching property of the phytoconstituents of \textit{G. lucidum}. GSH a well known antioxidant provides major protection in oxidative injury participating in the cellular system of defense against oxidative damage. In the present study, the decrease in tissue GSH content and SOD activity in liver may be due to its consumption during the oxidative stress induced by \(\gamma\)-irradiation. Zhao \textit{et al.}, (2006)\(^{(42)}\) reported that, mice bearing tumors showed decreased activity of SOD and this may be due to the loss of Mn\(^{2+}\) containing SOD activity in tumor cells and the loss of mitochondria leading to a decrease in total SOD activity in the liver.

In the present study, EST bearing mice showed significant increase in serum AFP and IL-2 concentrations compared to normal control. AFP is a commonly used tumor marker in detection of hepatocellular carcinoma \((43)\). Furthermore, AFP is not only used for diagnosis, but also is related to tumor size \((44)\). \textit{G. lucidum} significantly reduced the elevated levels of AFP and IL-2 in EST treated mice. The modulating effect of \textit{G. lucidum} may be due to the antioxidant and the free radical quenching property of its phytoconstituents. The polysaccharides isolated from mycelia of \textit{G. lucidum} inhibited the growth of S-180 in Balb/c mice and Kunming mice, with an inhibitory rate of 37.8 % -78.1 % \((45)\). \textit{G. lucidum} polysaccharide was also able to prolong the life-span of Lewis carcinoma-implanted C57BL/6 mice and promote anti-tumor activities of
cytotoxic drugs and chemical immunomodulators \(^{(46)}\). The triterpenoid fraction of the fruit bodies of *G. lucidum* also inhibited not only the primary solid tumor growth in the spleen and liver metastasis but also the secondary metastatic tumor growth in the liver in Lewis lung carcinoma (LLC)-implanted mice \(^{(47)}\). Lin and Zhang (2004)\(^{(17)}\) reported that, either *G. lucidum* or its active component has anti-tumor activity in mice in *vivo*, and its polysaccharides have synergic effect on the anti-tumor activity of cytotoxic drug such as cyclophosphamide.

Ionizing radiation-induced damages to cellular DNA is of prime biological significance. The types of damage suffered by DNA as a result of ionizing radiation include strand breaks of single and double strand types, base damage, elimination of bases, and sugar damage. Alkaline comet assay is a sensitive method by which DNA strand breaks at a single cell level can be monitored \(^{(48)}\). The comet assay results of tumor tissues in EST-bearing mice showed that, administration of *G. lucidum* prior to whole-body \(\gamma\)-radiation significantly induced % of DNA in tail, tail moment, and tail migration, in tumor cells. The present results would indicate that there could be a preferential damage in DNA and membranes in tumor cells when tumor-bearing mice were exposed to \(\gamma\)-irradiation after the administration of *G. lucidum*.

Gopakumar *et al.* (2010)\(^{(49)}\) found that oral administration of *G. lucidum* extract to tumor bearing mice along with exposure to gamma radiation result in tumor regression. They found significant reduction in radiation-induced damage to cellular DNA in normal tissues compared to the tumor, indicating preferential protection to normal tissues and possible use as an adjuvant in radiotherapy, for tumor regression and prevention of radiation-induced cellular damage in normal tissue \(^{(49)}\).

Anticancer effects of *G. lucidum* have been reported largely from in *vivo* experiments, and data from trials have been published. It is generally accepted that the anticancer effects are due to immune enhancement \(^{(17, 50)}\) may be exhibited from diverse chemical constituents \(^{(51, 52)}\). Experiments focused on the stimulatory effects of the higher molecular weight polysaccharides on the immune system \(^{(53-58)}\) and suppressive effect of the triterpenes (eg, ganoderic acid) on the growth and invasive behavior of cancer cells \(^{(53,58-60)}\). The present work revealed that *G. lucidum* might have anti-tumor properties and a radio-protective role in normal tissues as well as a radio-sensitizing effect in tumor tissues.
Acknowledgment

I would like to express my thanks and deepest gratitude to Prof. Dr Moustafa Elkabany, professor of pathology, National Cancer Institute, Cairo University, for his helpful role during the histopathological work.

REFERENCES


تأثير فطر الجينودرما لوسيديم على خلايا الكبد في الفنران المحملة بورم إرايخ
الصلب والعرضة للأشعة الجامية.

سحر إسماعيل إبراهيم* - حنان أحمد القياني**
قسم بحوث البيولوجيا الإشعاعية - قسم البحوث الصحية - المركز القومي لبحوث و تكنولوجيا الإشعاع
هيئة الطاقة الذرية. ص. ب. 29 مدينة نصر القاهرة.

تم إجراء هذه الدراسة للتحقق من قدرة فطر الجينودرما لوسيديم (فطر الريثي) (على مقاومة الأورام وزيادة كفاءة العلاج الإشعاعي وتحسين الانتشار الكبدية في الفنران المحملة بورم إرايخ المعروف). تم تجري علاج الفنران بمجملة 100 مليجرام/كيلوجرام من وزن الجسم (لمدة 15 يوما قبل و 15 يوما بعد تلقيح الورم) بシアست الفنران لجرعة جزءية للأشعة الجامية (2 جم/أيام). في اليوم الثامن من تلقيح الورم وصول حجم الورم حوالي 10 مليمتر تم تقييم الفنران إلى 6 مجموعات على النحو التالي: المجموعة الضابطة السليمة، مجموعة تلقت جرعات فطر الجينودرما لمدة 30 يوماً متتالية، مجموعة حاملة للورم، مجموعة حاملة للورم ومعريضة للأشعة، مجموعة حاملة للورم ومعريضة وعلاج بفطر الجينودرما، مجموعة حاملة للورم مع علاج بفطر الجينودرما وعلاج بفطر الجينودرما.

تم ذبح خمسة فنران من كل مجموعة بعد آخر جرعة من العلاج. تم جمع عينات الدم وأزال كل من الكبد والورم الصلب للدراسات البيوكيميائية والباثولوجية. وقد وُحّدت الحيوانات المتبقية لتسجيل نسبة البقاء على الحياة وقياسات حجم الورم. أظهرت النتائج المخبرية أن نسبة خلايا ارخ الغيرة تزداد بزيادة تركيز الجينودرما المضاد. كما أوضحت النتائج أن معالجة الفنران المحملة بورم إرايخ مع علاج بفطر الجينودرما وعلاج بفطر الجينودرما كانت على حد سواء (زيادة نسبة البقاء على الحياة ونقص في حجم الورم مقارنة بالمجموعة المحملة بالورم). وتبين من البحث وجود ارتفاع في نشاط وظائف الكبد المحملة في الترنس أمينيز وخلايا كية وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروjinيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجينيز وخلايا ديميدروجيني

وقد أدى تناول فطر الجينودرما إلى تحسين النتائج التي تناولت الفنران المحملة بورم إرايخ لتعريض الأورام دون استخدام العلاج الإشعاعي. وفي نسيج الورم، عاكس ذلك يمكن أن تتنقل إلى احتمالية كفاءة فطر الجينودرما المضادة للورم والوقاية للخلايا السليمة من التعرض الإشعاعي. يضاف إلى ذلك، فطر الجينودرما يسهم في زيادة كفاءة العلاج الإشعاعي.