

Radiomodifying Potential of *Panax ginseng* in Liver of Swiss Albino Mice against Gamma Radiation

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Abstract : *Panax ginseng* occupies an important role in the folk medicine of China, Korea and Japan. The present study was undertaken to determine the radioprotective efficacy of ginseng root extract in the liver of Swiss albino mice. The animals were divided into 4 groups. Group I-Only vehicle was administered. Group II-The animals received 10 mg/kg body weight ginseng root extract i.p. for 4 consecutive days. Group III-Animals were irradiated with 8Gy gamma radiation at the dose rate of 1.69 Gy/min at the distance of 80 cms. Group IV-Animals were given by ginseng root extract (10 mg/kg body weight) continuously for 4 days and on 4th day they were irradiated with 8 Gy gamma radiation after 30 min. The animals from above groups were autopsied on 1, 3, 7, 14 and 30 days. Biochemical estimations of phosphatases (acid & alkaline), LDH (lactate dehydrogenase), LPO (lipid peroxidation) and GSH (reduced glutathione) in liver and SGOT (serum glutamate oxaloacetate transaminase), SGPT (serum glutamate pyruvate transaminase) and alkaline phosphatase in serum were done. In ginseng treated group acid phosphatase (ACP), alkaline phosphatase (ALP), LPO and LDH in liver and SGOT, SGPT and alkaline phosphatase in serum did not show any significant alteration. However, a significant increase in GSH content in liver was recorded. In irradiated group there was a significant increase in ACP, ALP and LPO content in liver and SGOT & SGPT in serum was noted. Whereas, a significant decrease was recorded in GSH and LDH activity in liver and alkaline phosphatase activity in serum. Pretreatment of ginseng with radiation significantly alters the biochemical parameters in liver and serum. A significant decline in ACP, ALP activity and LPO content in liver and SGOT and SGPT activity in serum was observed. However, a significant increase in GSH content and LDH activity in liver and ALP activity in serum was estimated. The present study suggests that pretreatment of ginseng before irradiation significantly protects the liver and maintains the enzyme activity.

Key words : Liver, ginseng, phosphatases, radioprotection, lipid peroxidation, glutathione, Swiss albino mice

INTRODUCTION

Today ionizing radiation and radioactive isotopes have become powerful tool to treat various diseases including cancer. However, killing of tumor is not difficult, it is important to save the normal cells. Hence if radioprotective agents are combined with radiotherapy there could be a possibility to differentially protect the normal cells and kill the tumor cell. Many of synthetic compounds such as 2-mercaptopyrionyl glycine,^{1,2,3)} WR-2721,⁴⁾ lipoic acid,⁵⁾ deoxyspergualin,⁶⁾ and adenine monophosphate⁷⁾ have been tested for their protective action against radiation. But, they have their limited use due to their inherent toxicity.

Various plant extracts such as Spirulina,⁸⁾ Garlic,⁹⁾ Mentha¹⁰⁾, Aloe,¹¹⁾ and Ocimum¹²⁾ are being investigated to evaluate their radioprotective effects. Plants products appear to have an advantage over the synthetic compounds in terms of low/no toxicity at the effective doses.

Panax ginseng (Family- Araliaceae) is well known as an herbal medicine and has been used in therapy for thousand of years. It has been used in traditional chinese medicine for their important therapeutic qualities. Its roots are used for the extraction purpose. The pharmacological effects of ginseng have been demonstrated in the cardiovascular, immune, endocrine and nervous systems. Ginseng is also acclaimed as a haemopoietic stimulant, biomodulation, antistress and antiageing activities.^{13, 14, 15)}

Our earlier studies have shown that ginseng root extract significantly protect the testicular lesions against gamma radiation.¹⁶⁾ The present study was extended further to investigate the role of *Panax ginseng* root extract in pro-

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Table 1. Showing detailed explanation on the survival test results

Treatment	Initial No. of Mice	MSD (mean.)	T/C (%)
Radiation	50	18.79	328.15
Radiation+Ginseng	50	61.66	

etecting gamma radiation induced liver damages in Swiss albino mice.

MATERIALS AND METHODS

Animals: Random-bred, male Swiss albino mice (6-8 weeks old) were obtained from animal facility, IVRI, Izatnagar. They were kept under controlled environment conditions with provision of a 12 hrs. light : 12 hrs dark regimen. The animals were provided with pelleted standard mice feed (Hindustan Lever Ltd., INDIA) and tap water *ad libitum*.

Irradiation Source: Animals were irradiated by ^{60}Co source (ATC-C9) at the Cancer Treatment Centre, Radiotherapy Department, S.M.S. Medical College and Hospital, Jaipur. The animals were exposed to 8Gy whole body gamma radiation at a dose rate of 1.69 Gy/min at a distance of 80 cms from the source.

Ginseng Extract: The crude ginseng root extract was obtained from Amsar Pvt. Ltd., Indore (INDIA) in powder form. It was redissolved in DDW and administered i.p.

Experimental Protocol

The animals Swiss albino mice were divided into the following four groups:

Group I (n=30): Only vehicle (DDW) was given to these animals (served as Control).

Group II (n=30): The animals were administered 10 mg/kg body weight *Panax ginseng* root extract in DDW for 4 consecutive days intraperitoneally.

Group III (n=30): The animals were exposed to 8 Gy gamma radiation at once.

Group IV (n=30): The animals were administered ginseng extract 10 mg/kg body weight i.p. for 4 days and on 4th day they were irradiated with 8 Gy gamma radiation after 30 min. of extract administration.

The animals from the above groups were autopsied at 1,3,7,14 and 30 day after the treatment. The liver was excised and processed for GSH,¹⁷⁾ LPO,¹⁸⁾ LDH,¹⁹⁾ Alkaline and Acid phosphatase estimation.²⁰⁾

Liver Function Tests: To assess the liver function,

blood from autopsied animals was collected by cardiac puncture and serum was separated. The serum was processed for SGOT, SGPT²⁰⁾ and alkaline phosphatase activity.²²⁾

Survival Assay: Mice exposed to whole body 8Gy gamma radiation with or without ginseng pretreatment were checked daily for 30 days. The survival percentage of mice up to 30 days of exposure was determined.

Statistical Analysis: Data are expressed as Mean \pm S.E. Statistical significance of difference between groups was determined by Student's t-test.

RESULTS AND DISCUSSION

Survival assay

In the present investigation, it was observed that pretreatment of ginseng extract significantly enhances the survival percentage of mice exposed to 8Gy gamma radiation. In the irradiated group only 30% animals were survived upto 30 days. Whereas, in ginseng pretreated group 80% animals were survived. By the help of regression analysis, it was observed that Median survival day of only radiation treated group was 18.79 and for ginseng + radiation treated group median survival day was 61.66 (Fig. 1, Fig. 2).

Enzymatic assay

The present investigation revealed a significant increase in activities of acid phosphatase, alkaline phosphatase and lipid peroxidation level in liver and SGOT and SGPT activity in serum following radiation exposure.

Acid phosphatase is localized in cellular lysosomes and irradiation causes peroxidation of lysosomal membrane. Increased acid phosphatase activity in liver may be attributed due to breakdown of lysosomal membrane and liberation of the enzyme. Present studies are in agreement of the findings of Jacob and Maini,²³⁾ Samarth *et al.*,¹⁰⁾ and Kumar *et al.*,¹⁶⁾ Increased activity may also be due to synthesis of new lysosomes as consequences of radiation exposure (Fig. 3).

Alkaline phosphatase in the liver is closely connected with lipid membranes in the canalicular zone. Pathologically, the increase in its activity, suggests hepatobiliary disorders. In the present study, an increase in the alkaline

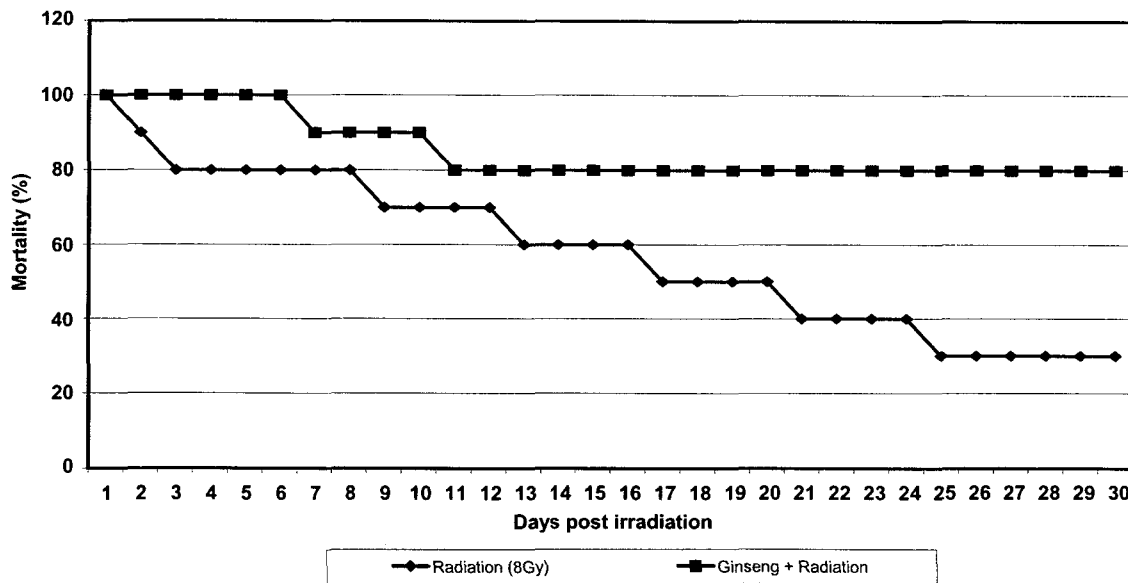


Fig. 1. Survival percentage in different experimental group.

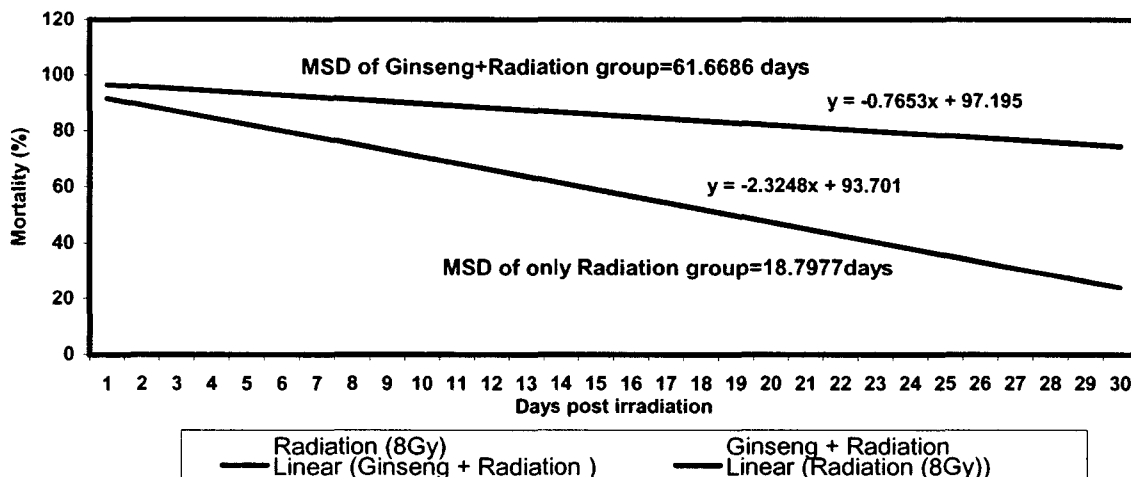


Fig. 2. Medium survival days in different experimental group.

phosphatase activity in the hepatic tissue may be due to the hepatocyte damage by radiation exposure (Fig. 4). The present study is in agreement with the findings of Yanardarg *et al.*²⁴⁾

A significant elevation in hepatic lipid peroxidation level in terms of TBARS (thiobarbituric acid reactive substances) or MDA (malondialdehyde) level was observed following radiation exposure. The basic effect of radiation on cellular membranes is believed to be the peroxidation of membrane lipids. Radiolytic products, including hydroxyl and hydroperoxyl radicals can initiate lipid peroxidation.^{16, 25, 26)} Lipid peroxidation has been suggested as one of the main causes of radiation induced membrane damage.²⁷⁾ UmaDevi and Ganasaundari¹²⁾ also observed that radiation exposure sig-

nificantly increases the lipid peroxidation.

The radiation exposure significantly elevated the serum aminotransferases (SGOT and SGPT). The excessive production of free radicals and lipid peroxides might have caused the leakage of cytosolic enzymes from the liver such as aminotransferases in the serum. These findings are in agreement with the findings of Sridharan and Shyamaladevi,²⁸⁾ and Hwang *et al.*²⁹⁾

Further, there was a highly significant decline was recorded in GSH level and LDH activity in liver and alkaline phosphatase activity in serum of irradiated animals at all autopsy intervals (Fig. 5, Fig. 7).

In the present investigation, serum alkaline phosphatase was found to decline after irradiation at all the intervals

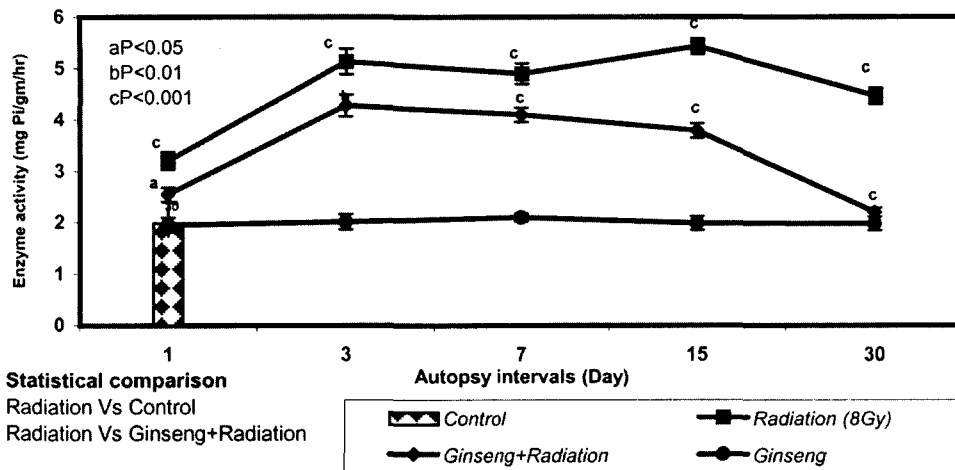


Fig. 3. Variation in liver acid phosphatase activity in different experimental groups.

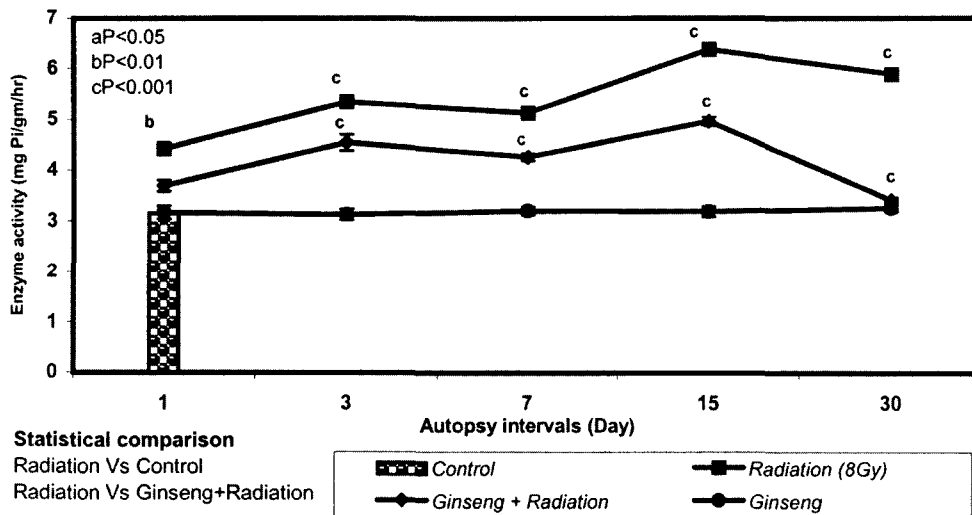


Fig. 4. Variation in liver alkaline phosphatase activity in different experimental groups.

studied. This is in agreement with the findings of Jacob and Maini,²³⁾ and Samarth *et al.*¹⁰⁾ They reported that deterioration in serum alkaline phosphatase activity in mice after irradiation with 5 and 8 Gy gamma rays respectively. Lynn and Skinner,³⁰⁾ observed non-exponential losses of activity in alkaline phosphatase after gamma radiation and suggested radical attack on phosphatase at centers of secondary importance for the enzymatic activity and there was a notable destruction of the component amino acid residue during radiolysis.

Alkaline phosphatase plays an important role in the maintenance of cell permeability and acts on monophosphoesters. The reason for the lower activity of serum alkaline phosphatase in the irradiated mice may be attributed to severe damage to the hepatocytes and GI tract.

The lesions affecting the villi are reflected in the

decreased enzyme activity.³¹⁾ The post irradiation reduction in alkaline phosphatase activity may be due to damage of brush border cells and increased permeability of villi cells (Fig. 8).³²⁾

In the present investigation radiation exposure induces significant decline in lactate dehydrogenase (LDH) activity in the liver. The enzyme LDH catalyzes the inter-conversion of lactate and pyruvate in the glycolytic pathway. For most study of toxicity, LDH release is a convenient screening method to assess irreversible cellular injury.³³⁾ The decreased activity of LDH following irradiation may be due to damage of liver cells thus, leakage of LDH from the hepatocytes into the serum. So, tissue concentration of LDH is decreased (Fig. 5).²⁸⁾

The GSH detoxification system is an important part of cellular defense against a large array of injurious agents.

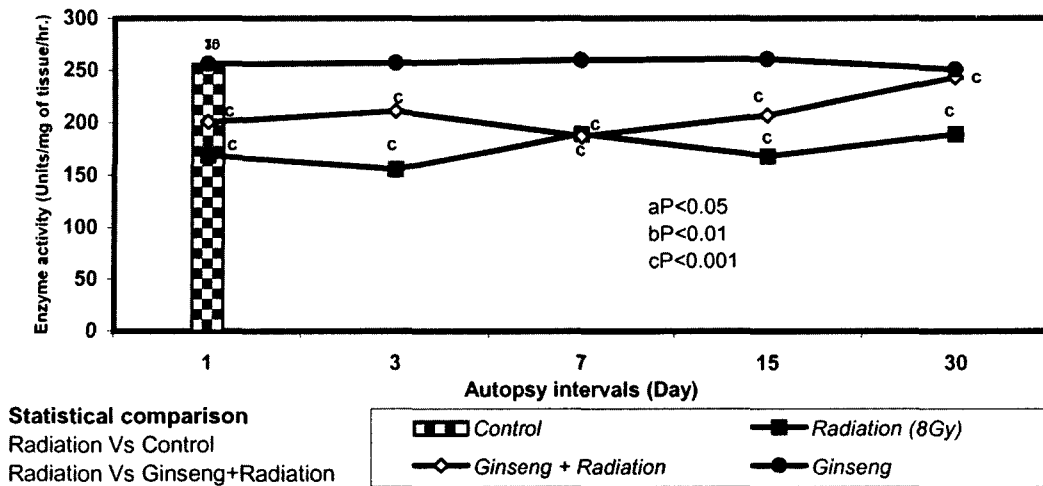


Fig. 5. Variation in Liver LDH activity in different experimental groups.

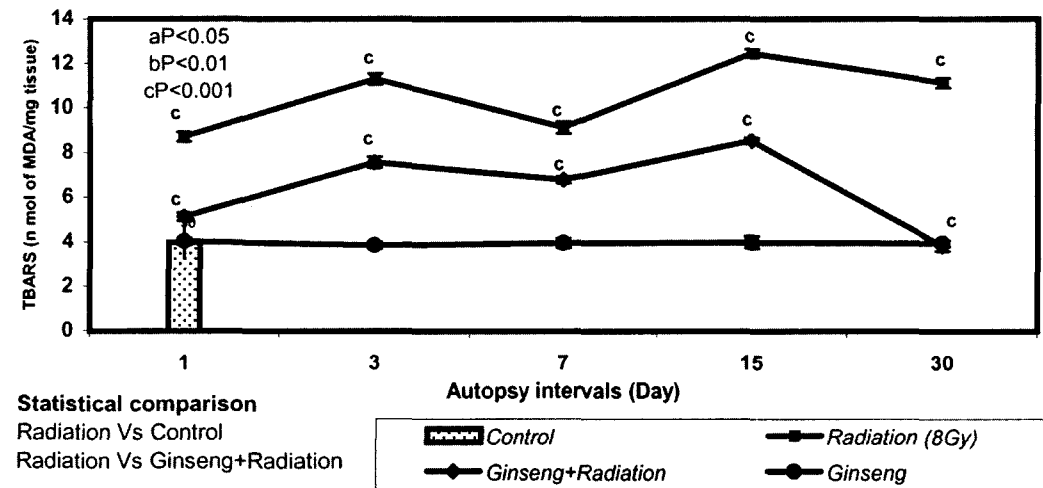


Fig. 6. Variation in hepatic lipid peroxidation content in different experimental groups.

GSH offers protection against oxygen derived free radicals and cellular lethality following exposure to ionizing radiation.³⁴⁾ Radiation interacts with biological molecules and produces toxic free radicals leading to DNA and membrane damage. Under normal conditions the inherent defense system, including glutathione and the antioxidant enzymes protects against oxidative damage (Fig. 6).

The present study demonstrated a significant reduction in GSH content in the radiation treated group. This could be due to enhanced utilization of the antioxidant system in an attempt to detoxify the free radicals generated by radiation (Fig. 7).

There appears to be a close correlation between depletion of GSH and elevation in lipid peroxidation. Under normal conditions the antioxidant defense system of the body protects against free radicals and oxidative stress.^{35, 36)} How-

ever, the oxidative stress due to the radiation induced free radicals can cause a dramatic fall in the hepatic GSH and overwhelm the cellular defense and lead to membrane lipid peroxidation and loss of protective thiols.^{12, 37-39)}

In the present investigation, it has been observed that *P. ginseng* extract provided protection by exhibiting a significant increase in acid phosphatase, alkaline phosphatase activity and LPO content in liver and SGOT and SGPT activity in serum (Fig. 9, Fig. 10) and significant increase in GSH content and LDH activity in liver and alkaline phosphatase activity in serum at various periods of study in experimental animals compared with the respective control.

Most pharmacological actions of ginseng are attributed to ginsenosides, which can act in a wide range of tissues. Among all ginsenosides, ginsenosides Rf, Rb₁₋₂ and Rg₁

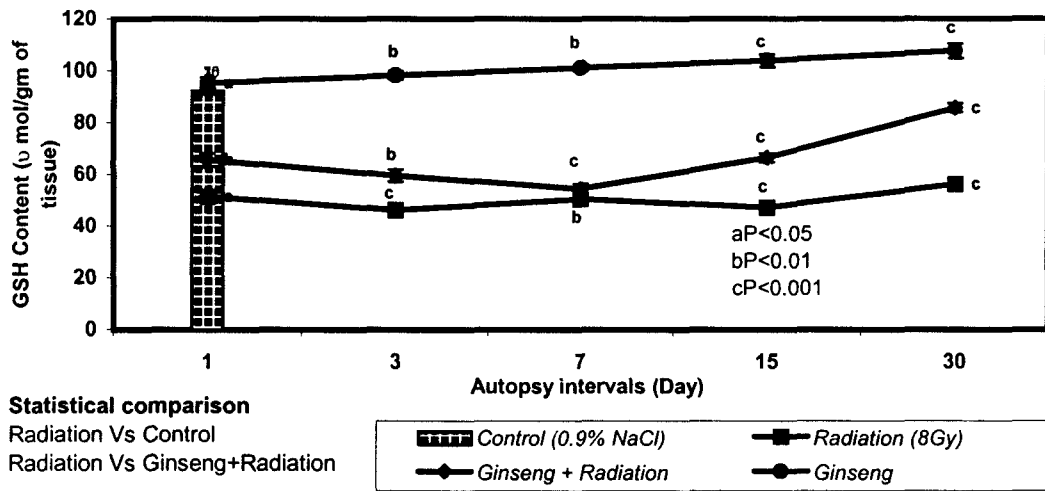


Fig. 7. Variation in liver GSH content in different experimental groups.

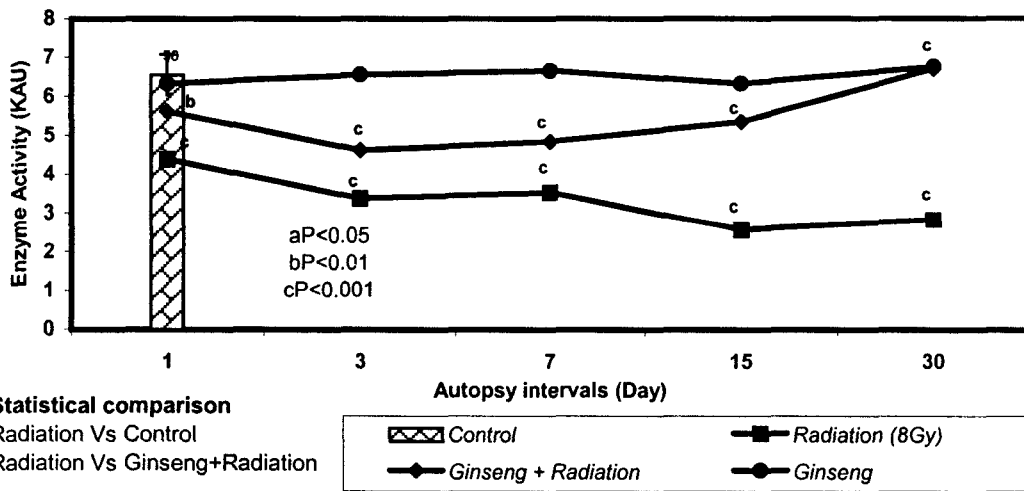


Fig. 8. Variation in serum alkaline phosphatase activity in different experimental groups.

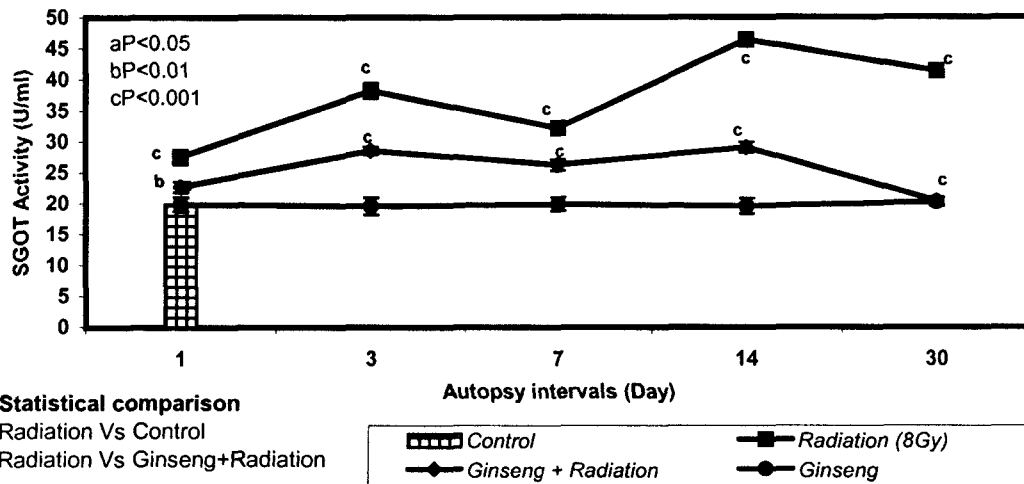


Fig. 9. Variation in SGOT activity in different experimental groups.

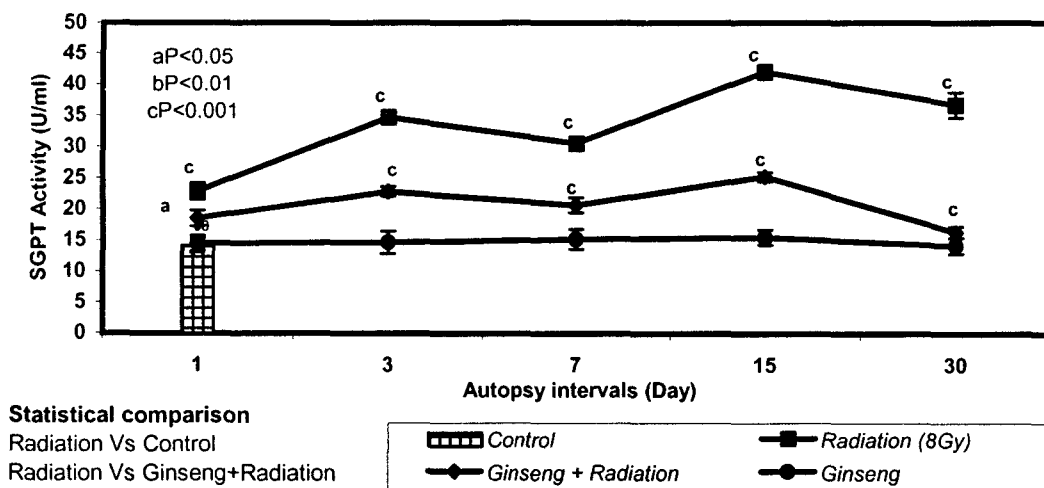


Fig. 10. Variation in SGPT activity in different experimental groups.

are the most abundant.⁴⁰⁾

The medicinal efficacy of ginseng against gamma radiation may be closely linked with its protective properties against free radical attack.⁴¹⁻⁴⁴⁾

The significant reduction in the level of lipid peroxidation by ginseng pretreatment clearly demonstrated that ginseng protects the membranes against radiation induced oxidative damage. Ginseng given before irradiation significantly elevated the GSH levels. It brings about significant decreases in lipid peroxidation content. It suggests that ginseng protection may be mediated through modulation of cellular antioxidant potential. The increased GSH levels by ginseng will facilitate reduction of oxidative free radicals by H donation thus reduces cellular damage.

Ginseng extract was also reported to scavenge superoxide radicals⁴⁵⁾ and inhibit lipid peroxidation through transition metal chelation⁴⁶⁾ to diminish oxidative DNA damage caused by fenton reagent.⁴⁷⁾ The active role of ginseng extract scavenging hydroxyl radical and protecting unsaturated fatty acids may contribute to stabilize the structure of lipids membrane perturbed by free radical attack.⁴⁶⁾ Thus, reduces membrane damage.

Kim et al.,⁴⁸⁾ also reported that water fraction and alkaloid fraction of ginseng may reduce cell damage, especially the damage to DNA molecules, caused by gamma rays and thus playing a role in the regeneration process of damaged cells. It is possible that ginseng reduces DNA damage by antiradical action.

To conclude, the present study demonstrated that deleterious reactive oxygen species or free radicals or lipid peroxides responsible for radiation induced liver damage may be alleviated by ginseng root extract treatment.

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