Life on earth has evolved under continuous and gradually diminishing exposures to cosmic radiation, charged high energy particles, as well as to terrestrial $\alpha$, $\beta$, and $\gamma$-rays. Large populations all over the globe now live in an environment contaminated by radiations from both natural and man-made sources. The origins of various types of natural background radiation are solar emissions of nuclear particles, nuclear reactions of these particles with the earth’s atmosphere, and by the radioactive decay of very long lived radioisotopes distributed throughout the earth’s crust. These radioactive isotopes include potassium-40, uranium, and the noble gas radon and its decay products. Man made background radiation sources include radiation from nuclear weapon testing, nuclear power station accidents, emissions from burning fossil fuels such as coal fired power plants, emissions from nuclear medicine facilities and patients, emissions from radiological imaging and therapy. These radioactivity exposures are accompanied by unavoidable or accidental releases of radioactivity into the environment which cause global environmental and health consequences in both military personnel and civilian populations.

Radioactivity exposures also occur in nuclear emergency workers or liquidators who bury the melting reactor core. Military personnel (Atomic soldiers) are exposed to ionizing radiations especially during nuclear installation periods. Epidemiologic studies of thousands of Uranium miners in various countries have revealed increased mortality risk factors and lung cancer deaths. Airline crews are subject to cosmic irradiation consisting of neutrons and high energy $\gamma$ rays. A cancer mortality and incidence study among Canadian male pilots showed significant excess rates for several cancers, including Hodgkin’s disease and nonmelanoma skin cancer (Band et al, 1990). Further there are several reports of mutational effects in radiotherapy technicians. Significantly elevated risks for leukemia and various cancers were found among Chinese radiologic workers (Wang et al, 1990). Cancer patients are exposed to ionizing radiation during radiotherapy. Radiotherapy is the use of ionizing radiation for the treatment of cancer and it is one of the most effective treatments for cancer (Steel, 2002). Eighty percent of cancer patients need radiotherapy at some time or other either for curative purposes or palliative purposes (Nair et al, 2001).
Radiotherapy involves both external beam radiotherapy and brachytherapy. Treatment choice depends on the type of tumor and location within the body. The dose of radiation is determined by the intent of the therapy (i.e., curative or palliative), the volume of the tumor, the relative radiosensitivity of the tumor cells and expected toxicity to the surrounding normal tissue. Most curative radiotherapy regimens consist of daily treatments or fractions in the range of 1.8 to 3 Gy per day over a period of 5 to 8 weeks. The intent is to achieve local control of the tumor to prevent further local tissue destruction, organ failure, and the seeding of secondary metastasis. Palliative radiotherapy is given in order to achieve better pain control, to control bleeding or to prevent tissue destruction or ulceration. These radiotherapy treatments are usually of short duration and consist of 1 to 3 fractions of 5 to 8 Gy or 5 to 10 fractions of 3 to 4 Gy. However, radiotherapy has achieved limited success in eradicating cancer. One major reason for this stems from the fact that normal and cancerous tissues have similar responses to radiation exposure (Mitchell et al, 2000). Consequently, radiation-induced injury may present during radiotherapy treatment or some time later after the completion of radiotherapy. The acute and chronic side effects that may occur following local radiotherapy are directly linked to the normal structures and tissues within the irradiated volume.

**Consequences of radiation exposure to general population**

Medical X ray exposure presents a source of radioactivity to civilians. Recent studies conclude that background and medical radiation induce about 25% of all “spontaneous cancers” in the population (Gofman 1990). Medical X ray exposures over past decades can account for at least 75% of all female breast cancers (Gofman, 1996). This is due to the fact that tissues of female breast is about 2.5 times as sensitive to cancer induction as all other tissue taken together (Dohy et al, 1994). As a result young female children would be particularly sensitive to breast cancer induction from X-ray exposures. Another case of radioactivity exposure to civilians is by nuclear weapons production, testing and nuclear accidents as in recently exploded Fukushima plant. High doses of ionizing radiation from these nuclear explosions result in many serious health effects within hours, weeks or months (Lloyd et al, 1992: Loken, 1987). Another example of radioactivity
exposure to general population is that which occurs in atom bomb survivors. In these populations, cancer cases in excess of ‘normal’ background rates have been observed may be due to somatic effect of radiation. Among children of atom bomb survivors, nonmalignant congenital defects, such as abnormal brain development and small head size, have been related to a single prenatal exposure, down to doses less than 20 mGy (Yoshimaru et al, 1995). Further there is strong correlation between juvenile cancers with natural background radiation (Konx et al, 1988).

Intracellularly irradiation produces severe damaging events. A deleterious effect of radiation is the production of reactive oxygen species (ROS), which include superoxide anion ($O_2^-$, a free radical), hydroxyl radical (•OH), and hydrogen peroxide ($H_2O_2$) (Fang, 1991). These reactive species may contribute to radiation-induced cytotoxicity (e.g., chromosome aberrations, protein oxidation, and muscle injury) and to metabolic and morphologic changes (e.g., increased muscle proteolysis and changes in the central nervous system) in animals and humans. Many effects have been attributed to ionizing radiation (IR) induced damage to nuclear DNA or that occur following irradiation of the cytoplasmic compartment of cells. These can also occur in cells that have received no direct exposure to IR. These so-called ‘bystander effects’, i.e., radiation induced effects in unirradiated cells, include cell killing, increase in intracellular reactive oxygen species, the induction of mutations, enhanced cell growth, the induction of apoptosis, the induction of genomic instability and neoplastic transformation. Bystander effects occur when reactive radiation products or damage signals from a cell migrate to non-irradiated cells thereby producing biological effects (Grosovsky et al, 1996; Wu et al, 1999; Zhou et al, 2000). The risk of cell toxicity is increased with the application of more intensive radiotherapy techniques intended to increase tumor cell kill.

Traditionally the effects of radiation treatment on normal tissues have been divided, based on functional and histopathological end points into early (acute) responses, which occur within a few weeks of radiation treatment, and late response that may take many months or years to develop. Acute radiation effects
are caused by transient suppression of cell proliferation in tissues with a high rate of cell turn-over, such as the bone marrow, epidermis and the mucosal lining of the respiratory and digestive tracts (Bloomer and Hellman 1975). Late tissue responses occur in organs whose parenchymal cells normally divide infrequently and hence do not express mitosis-linked cell death. It has also been hypothesized that late radiation effects occur as a result of functional or structural damage to small blood vessels (capillaries, venules and arterioles) leading to disruption of blood supply to the tissues (Mathes and Alexander 1996). One common late reaction is the slow development of tissue fibrosis that occur in tissues such as muscle, lung, gastrointestinal tract etc. There is also a third category of intermediate effects to describe certain types of normal tissue damage that are first manifested about 2 - 4 months after the end of treatment e.g., radiation-induced pneumonitis, which may be mild and resolve spontaneously or may become severe and progress to pulmonary fibrosis (Chernecky and Sarna 2000).

Radioprotection
The potential application of radioprotective chemicals in the event of planned exposures or radiation accidents/incidents has been investigated from the beginning of the nuclear era (Weiss and Simic, 1988; Bump and Malaker, 1998). It has also been considered possible that radiation therapy for cancer patients could be improved by the use of radioprotectors to protect normal tissue. Because of the short life times of radiation induced radicals, radioprotectors have to be present in the cell at the time of irradiation. They are equally effective for tumor and normal cells in vitro. Thus specificity in vivo depends largely on preferential uptake of such agents into the normal tissue. In this regard, several compounds were tested for radioprotective efficacy. In recent years, a number of cytoprotective agents capable of protecting normal tissue against damage caused by either chemo- or radiotherapy have been investigated including amifostine (WR-2721), dexrazoxane, mesna, glutathione, and N-acetylcysteine. Among these, amifostine, dexrazoxane and mesna have FDA approval for use in cytoprotection. However only amifostine has been shown in clinical trials to reduce radiation induced toxicity.
Amifostine (WR2721), is a phosphorothioate compound that is converted into a sulfhydryl-containing compound in vivo by the action of alkaline phosphatase. It was developed by The Walter Reed Army Research Institute of United States Army with the memory of devastating effects of Nagasaki and Hiroshima following World war II. In 1996, the Food and Drug Administration (FDA) registered amifostine for use as a cytoprotective agent with cisplatin-based chemotherapy against ovarian cancer. More recently, a phase 3 study has provided strong evidence that amifostine prevents xerostomia in patients treated with radiotherapy for head and neck cancer. Based on this, the FDA approval was extended in 1999 to postoperative radiotherapy for head and neck cancer as well (FDA, 1999). It is also used to decrease the cumulative nephrotoxicity associated with platinum-containing agents. Further, studies of this compound in patients have shown substantial protection of normal tissue, including salivary gland, lung, and mucosa without detectable change in tumor response (Brizel et al, 2000; Antonadou et al, 2003). The selective uptake of this compound in normal tissue is believed to be due to poor penetration from tumor blood vessels and reduced levels of alkaline phosphatase in tumors.

Amifostine although can reduce radiation side effects but does not remove them completely. Further, these synthetic radioprotective agents have got several side effects within the body. Common side effects of amifostine include hypocalcemia, diarrhea, nausea, vomiting, sneezing, somnolence, and hiccoughs (Hensley, 1999). Serious side effects include: hypotension (found in 62% of patients), erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, immune hypersensitivity syndrome, erythroderma, anaphylaxis, and loss of consciousness (rare). Most patients receiving amifostine with radiotherapy require antimetics. These side effects are enough to limit the use of amifostine to doses lower than required to achieve maximal radioprotection.

Another approach that is used to protect the normal tissue against the development of late radiation effects is the use of steroids. This approach has been investigated experimentally, particularly for the prevention of late effects in lung and kidney. Usually the expression of angiotension converting enzyme (ACE) is increased in
lung and kidney at late times after irradiation. So agents which block ACE activity (e.g., captopril) or agents which block directly the action of angiotensin II have been found to protect lung and kidney from the development of radiation induced fibrosis and nephropathy. However, steroids only delay the development of symptoms rather than preventing them. There are some agents which protect the cells against radiation damages in \textit{in vitro} conditions. These include agents that can scavenge radiation produced radicals, such as dimethyl sulphoxide (DMSO) and those that can donate a hydrogen atom back to a radical site created on a macromolecule such as DNA, including the nonprotein sulfhydryls, glutathione, cysteine and cystamine (Patt 1949; Becq 1951). However, these compounds produced serious side effects and were found to be toxic at the doses required for radioprotection.

In this scenario, there is continued interest and need for the identification and development of effective and nontoxic radioprotective compounds. Many natural antioxidants, whether consumed before or after radiation exposure, are able to confer some level of radioprotection (Weiss and Landauer, 2000). There is evidence that “natural” antioxidants (superoxide dismutase, \textit{Gingko biloba} extract, and mixtures of antioxidant plant phenols, vitamins and minerals) may protect against long-term effects of radiation exposure occurring in human populations exposed to radiation. Besides these extracts, a large number of plants contain antioxidant phytochemical compounds that have been reported to be radioprotective in various model systems. These include green tea (polyphenols), dithiohlthiones, Compounds in \textit{Gingko biloba} extract such as flavone glycosides and terpene lactones, milk thistle (silymarin), curcumin, allicin in garlic, and lycopene. Emerit and coworkers described the appearance of clastogenic factors in the plasma of Chernobyl emergency workers (liquidators) and exposed children many years after radiation exposure and the suppression of these factors by antioxidant supplements (Emerit et al, 1995: 1997a: 1997b). Recent studies on the flavonoids orientin and vicenin extracted from \textit{Ocimum sanctum} revealed significant protection against chromosome aberrations and lethality when administered to mice at nontoxic doses before radiation exposure (Uma Devi et al, 1998; Uma Devi et al, 1999). Most of these botanical or alternative medicines would be
considered dietary supplements in the United States and would not be subject to strict regulation by the Food and Drug Administration.

Compounds with radioprotective activity from natural sources have attracted considerable attention due to their potential use and lack of toxicity (Arora et al, 2005; Kang et al, 2006). Mushroom is one of the useful, delicious and mysterious member of the biosphere (Verma et al, 1987a; 1987b). Because of their taste and fleshy construction, they have been paid the attention by mankind for ages. Today mushrooms are considered as alternative food source to provide adequate nutrition to world's increasing population. Mushrooms are very poor in lipid and very rich in protein, ash, fibre, and minerals. The antioxidants present in dietary mushrooms are of great interest as possible protective agents which help the human body to reduce oxidative damage without any interference (Adams and Wermuth 1999). Further, it has been known for many years that mushrooms belonging to Basidiomycetes fungi family have diverse effects against cancers of stomach, oesophagus, lungs etc. Especially presence of medicinal fungi useful against cancer is known in China, Japan, Korea as well as Russia, USA and Canada.

A number of bioactive molecules have been identified in many mushroom species including polysaccharides, terpenes, polyphenols, alkaloids, lectins, AHCC (Active Hexose Correlated Compound), Psilocybins etc. Among these, polysaccharides are the best known and most potent mushroom derived substances with immunomodulating as well as antitumor properties. In Japan, different mushroom polysaccharides are available which act as carcinostatics. It includes Lentinan from the fruit bodies of Lentinus edodes, Polysaccharide-K (PSK) and Polysaccharide-P (PSP) from the mycelium of Coriolus versicolor, Schizophyllan from Shizophyllum commune, Maitake D-fraction from Grifola frondosa etc. Further, more than 50 mushrooms species have yielded potential immunoceuticals which have anticancer as well as immunomodulating property.

**Mushrooms polysaccharides**

Polysaccharides are polymers of sugars (monosaccharides) joined to each other by glycosidic linkages which results in the formation of highly branched macromolecules. Usually polysaccharides have (1, 3) as well as (1,6) β-glycosidic
linkage with D-glucans as backbone. Together with chitin, the beta-glucans are components of mycetes' cell walls. A high level of biological efficiency has been found in beta-glucans, especially beta-1,3-D-glucans isolated from some basidiomycetes. Polysaccharides have significant capacity for carrying biological information due to a high potential for structural variability. They have attracted attention over the years because of their bioactive and medicinal properties.

Wasser (2002) reported that mushroom polysaccharides can be regarded as Biological Response Modifiers (BRM). This basically means that they cause no harm and place no additional stress on the body, but help the body to adapt to various environmental and biological stresses. Mushroom polysaccharides support some or all of the major systems of the body, including nervous, hormonal and immune systems as well as regulatory functions. Of significant relevance and importance is the ability of particular mushrooms-derived compounds to modulate the human immune response and to inhibit certain tumour growths (Wasser and Weis 1999; 1999a). These compounds, which appear to stimulate the human immune response, are being sought for the treatment of cancer, immunodeficiency disease or for generalized immunosuppression following drug treatment. They are also sought for combination therapy with antibiotics and as adjuvants for vaccines (Jang et al, 1997).

Recently, polysaccharides isolated from several mushroom spp. have received special attention due to their potent pharmacological properties such as anti-tumor (Bae et al, 2005; Han et al, 1999) and anti-inflammatory activity (Kim et al, 2003). Protein bound polysaccharide complex isolated from mushroom *Lentinus lepideus* (PG 101) had been reported to recover radiation induced bone marrow suppression very efficiently (Jin et al, 2003). Polysaccharides isolated from the *Phellinus gilvus* (PG) have various biological activities related to inflammation, including inhibition of pulmonary inflammation (Jang et al, 2004), prevention of intraperitoneal adhesion under infectious circumstances (Bae et al, 2004; Bae et al, 2004a; Bae et al, 2004b) and promotion of dermal wound healing in normal host (Bae et al, 2004c). Proteoglycans from a closely related species *P.linteus* had been reported to stimulate host defense immune system by boosting both humoral and cellular immune response (Kim et al, 2003). Polysaccharide protein complex from
a *P. linteus* stimulate immune system and enhance the production of interleukins (Kim et al, 2006). Polysaccharides isolated from medicinal mushrooms act as immunopotentiator and enhance immune status in the body by a variety of mechanisms including production of immune mediators like cytokines (Gi-Su-Oh et al, 2006). Hence they are excellent agents against radiation induced immunosuppression.

*Phellinus* species are mostly tropical mushrooms and 18 species are known from Kerala. *Phellinus linteus* is known to be extensively used in Chinese medicine (Ying et al, 1987). *Phellinus rimosus* is a parasitic host specific polypore macrofungus often found growing on jackfruit trees (*Atrocarpus heterophyllatus*) trunks (Leelavathy, 2000). Earlier investigations showed that ethyl acetate and methanol extracts of *P. rimosus* possessed antioxidant, antitumor and hepatoprotective activities (Ajith and Janardhanan 2001; Ajith and Janardhanan 2002; Ajith and Janardhanan 2003). Recent investigations have also demonstrated the profound antioxidant, anti-inflammatory and antiarthritic activities of polysaccharide protein complex (PPC-Pr) isolated from the aqueous extract of *P. rimosus* (Meera et al, 2009a; Meera et al, 2009b). However radioprotective properties of this mushroom have not been identified yet. Aim of this study is to investigate the radioprotective effects of *P. rimosus* derived components.