Radiation has helped life forms evolve, but also it manifests deleterious effects on life forms. Ionizing radiation causes a spectrum of biological effects in cells, of which the free radicals play the most significant role. Oxidative free radicals generated during the radiolysis of water are responsible for many of the detrimental effects of ionizing radiation in living systems as they virtually attack all components including DNA, protein and membranes causing their dysfunction and damage (Moller and Wallin, 1998; Hall, 1994) and impairs the indigenous cellular antioxidant defense system (Gracy et al., 1999). Ionizing radiation is currently being used in a large number of applications in therapeutic, diagnostic, industrial and other areas apart from for the generation of nuclear power and developing new varieties of high yielding crops, sterilization of materials for surgical and medical use and enhancing storage period of food materials. In many instances where radiation is used, the personnel manning the radiation sources may be subjected to low level exposures. High exposures to radiation may occur due to accidents (like Chernobyl, Mayapuri in Delhi, Fukushima catastrophe, etc) or during “nuclear wars”. Besides, radiation poses a major risk for astronauts especially for long-duration space flights. Further, radiotherapy is a dominant and effective mode of cancer treatment. Radiation injury to normal tissues surrounding the tumour is one of the major problems limiting the success of radiotherapy where the normal tissues are to be protected from the deleterious effects of radiation. Protection of biological systems from ionizing radiation is of paramount importance during accidental and unavoidable exposures to radiation (Upadhyay et al., 2005), and development of novel and effective approaches to combat radiation damages using non-toxic radioprotectors are of considerable interest for defense, nuclear industries, radiation accidents, space travels, etc, besides the protection of normal tissues during radiotherapy of tumours.

Many synthetic as well as natural compounds have been investigated for their efficacy to protect against radiation induced cellular damages. They include sulfhydryl compounds, antioxidants, plant extracts, immunomodulators, and other agents (Nair et al., 2001). Natural antioxidants strengthen the endogenous antioxidant defences from ROS ravage and restore the optimal balance by neutralizing the reactive species. They are gaining immense importance by virtue of their critical role in disease prevention. Dietary bioactive compounds and microelements from different functional foods, herbs and nutraceuticals can ameliorate or even prevent diseases (Ferrari 2004; Szentmihalyi et al. 2005). Most of the in vivo experiments performed support this
statement. Choi and Hwang (2005) showed that the intake of medicinal plants in rat diets results in an increase in antioxidant enzyme activity and high-density lipoprotein-cholesterol of serum, and in a decrease of malondialdehyde, which may reduce the risk of inflammatory and heart disease. Plants have long been regarded as having considerable health benefits, due to their main antioxidant compounds, phenolics (Sarni-Manchado et al. 2000; Caballero-George et al. 2002). A number of medicinal plants have shown radioprotective and radiorecovery effects, also been attributed to the antioxidant activities of phenolic compounds in them (Arora et al., 2005; Jagetia and Venkatesha, 2005). The beneficial effects of phytophenols are mainly attributed to their antioxidant properties, since they can act as chain breakers or radical scavengers depending on their chemical structures (Rice-Evans, 2001). Phytophenols might also trigger changes in the signalling pathways and subsequent gene expression (Chen, 2002; Pfeilschifter, 2003). It is possible that the distinct chemical and receptor-mediated activities of phenolic compounds might result in similar outcomes via different pathways. Under some circumstances, phytophenols can exhibit pro-oxidative effects (Weiss and Landauer, 2003).

The use of materials in nanoscale provides unparalleled freedom to modify fundamental properties such as solubility, diffusivity, blood circulation half-life, drug release characteristics, and immunogenicity. These nanoscale agents may provide more effective and/or more convenient routes of administration, lower therapeutic toxicity, extend the product life cycle, and ultimately reduce health-care costs. As therapeutic delivery systems, nanoparticles allow targeted delivery and controlled release. In the last two decades, a number of nanoparticle-based therapeutic and diagnostic agents have been developed for the treatment of cancer, diabetes, pain, asthma, allergy, infections, and so on (Brannon-Peppas and Blanchette, 2004; Kawasaki and Player, 2005). Recently, nanoparticles are gaining interest in the field of radioprotection, as cerium oxide nanoparticles, yttrium oxide nanoparticles, carbon nanoparticles, etc. were found to possess antioxidant properties and several works have shown the ability of these nanoparticles to offer protection against radiation damages (Rzigalinski, 2005; Rzigalinski et al., 2006; Ali et al., 2004; Mirkov et al., 2004; Tarnuzzer et al., 2005; Djordjevic et al., 2005; Daroczi et al., 2006; Schubert et al., 2006; Das et al., 2007; Trajkovic et al., 2007; Colon et al., 2010). Nanoparticles due to the electron clouds that surround them could have high reactivity with free radicals (Bhatia, 2008).

Sesamol (SM) is known to be an antioxidant contained mainly in processed sesame oil (Fukuda et al., 1986). It has been known for many years that sesame oil is highly resistant to oxidative deterioration as compared to other edible oils (Mohamed and Awatif, 1998). SM is formed from
decomposition of sesamolin during the processing of sesame oil. Sesamol has a phenolic and a benzodioxole group in its molecular structure. The phenolic groups of molecules are generally responsible for the antioxidant activity of many natural products (Wright et al., 2001; McPhail et al., 2003; Joshi et al., 2001, 2002). Sesamol has been found to inhibit lipid peroxidation, hydroxyl radical-induced deoxyribose degradation, and DNA cleavage (Joshi et al., 2005). In Swiss albino mice, scavenging the free radicals, activating the endogenous antioxidant enzymes (GSH, GST, catalase), protecting the hemopoietic system, and preventing DNA damage are likely to be the mechanisms for the radioprotective activity of sesamol (Parihar et al., 2006). On the other hand, benzodioxole derivatives are widely distributed in nature and have been shown to possess anti-tumour, antioxidant, and many other biological activities (Mazzio et al., 1998; Tseng et al., 2001; Tagashira and Ohtake, 1998; Jurdi et al., 1987). These activities have been attributed to the effect on various enzymes and the scavenging of reactive oxygen species.

Gallic acid (GA), a polyhydroxylphenolic compound, is widely distributed in various plants, fruits and foods. GA and its derivatives are present in gallnuts, oak bark, sumac, grapes, and tea leaves as one of the main phenolic components (Ow and Stupans, 2003). It also occurs as a free molecule or as one of the chemical components in tannin (Hemingway et al., 1992). Gallic acid is a strong natural antioxidant and has been pharmacologically active as anti-bacterial, anti-melanogenic, anti-viral and anti-inflammatory, besides anti-cancer activity in various cancer cells (Kang et al., 2008; Kratz et al., 2008; Kim et al., 2006; Ji et al., 2009; Inoue et al., 2000; Faried et al., 2007). It is also employed as an antioxidant in food, in cosmetics and in the pharmaceutical industry (Gali et al., 1992; Fiuza et al., 2004; Sameermahmood et al., 2010). As far as the toxicity is concerned it has an LD50 dose of 5 g/kg body weight in rats (Shahrzad et al., 2001).

Silver has had some medicinal uses going back for centuries. The Phoenicians are said to have stored water, wine, and vinegar in silver bottles to prevent spoiling. Prior to the introduction of antibiotics, colloidal silver was used as a germicide and disinfectant (Alexander, 2009). Silver nanoparticles are known to possess excellent free radical scavenging and anti-inflammatory activities (Banerjee and Narendhirakannan, 2011; Bhol and Schechter, 2007; Nadworny et al., 2010, 2010a; Wong et al., 2009). Previous studies from our lab have explored the radioprotecting properties of silver nanoparticle complexes of compounds such as glycyrrhizic acid (Chandrasekharan et al., 2011), α-lipoic acid acid (Ramachandran and Nair, 2011) and 6-palmitoyl ascorbic acid 2-glucoside (Chandrasekharan et al., 2011a).
Sanazole or AK-2123 (AK) is a nitrotriazole derivative hypoxic cell sensitizer with lower neurotoxicity than most nitroimidazoles (Shibamoto *et al.*, 1986). Experimental data and various clinical studies demonstrated AK as a potential radio and chemosensitizer (Garcia-Angulo and Kagiya, 1992; Huilgol *et al.*, 1996). High antimetastatic activity, potent chemosensitizing with cisplatin and immunomodulatory effects was also reported for sanazole (Konovalova, 2003).

The anthracycline derivative doxorubicin (DOX) is a very potent drug with broad spectrum of biological activity. DOX is isolated from cultures of *Streptomyces peucetius* and is used in the management of various hematological malignancies and other neoplastic diseases. The Clinical efficacy of drug in a wide range of malignant disorders is hampered by its dose limiting side effect cardiotoxicity. The most serious long-term side effects are dilated cardiomyopathy and congestive heart failure. The hypothesis for doxorubicin-induced toxicity is based on the formation of reactive oxygen species (ROS), such as superoxide and hydrogen peroxide, by reactions catalyzed by the quinone moiety of doxorubicin. Further, membrane lipid per oxidation, mitochondrial damage, and iron-dependent oxidative damage to macromolecules, histamine release and disruption of calcium homeostasis are also implicated in the mechanism of drug related side effects. It was supposed that administration of a potent antioxidant and protective drug therapy together with a chemotherapeutic agent may be the proper advance to reduce the toxic side effects of drug.

*Ganoderma lucidum* is an important medicinal fungus belonging to the Ganodermataceae family which has been popularly used for its health promoting properties (Stapleton *et al.*, 1996; Thornton *et al.*, 1998; Wasser and Weis, 1999). It is consumed more for its pharmaceutical rather than nutritional value. *G. lucidum* extract (GLE) has been used for long time in China to prevent and treat various human diseases such as hepatitis, hypertension, and hyperglycemic, tumorigenic and immunological diseases (Kim *et al*., 1999; Gao *et al*., 2005; Kimura, 2005). The effects of GLE on cancer, hypertension, hypercholesterolemia, and hepatitis have been demonstrated by several studies (Franz, 1989; Furusawa *et al*., 1992; Wang *et al*., 1997). *G. lucidum* was reported to contain some intensely bitter compounds including lucidenic acid A, B, C, D, E, lucidone A, and ganoderic acids B, which are known to inhibit both histamine release from mast cells and an angiotensin converting enzyme that is responsible for hypertension and growth of liver cancer cells (Nishitoba and Sato, 1985; Kohda *et al*., 1985). *G. lucidum* was also reported to contain polysaccharides and protein-bound polysaccharides that have anti-tumour properties, antihypertensive activities, and also causes decrease in blood glucose level (Kim *et al*., 1999; Miyazaki and Nishijima, 1981; Hikino *et al*., 1985).
The present study focuses on (i) The evaluation of radioprotective, chemoprotective and anti-tumour activities of phytophenolic compounds– (a) Sesamol (SM) and its Silver nanoparticle complex SNSM, and (b) Gallic acid (GA) and its Silver nanoparticle complex SNGA. Their usefulness as adjuvants in tumour radiotherapy and chemotherapy is also explored. (ii) The Silver nanoparticle (SN) complexing of hypoxic cell sensitizer Sanazole (AK), chemotherapeutic Doxorubicin (DOX) and their combinations (SN-AK, SN-DOX, AK-DOX and SN-AK-DOX) for enhanced anti-tumour efficacy is investigated. (iii) The evaluation of hemi-alcoholic extract of medicinal mushroom *Ganoderma lucidum* (GLE) as an adjuvant in tumour- radiotherapy is also looked into.