Protecting living beings from onslaughts of ionizing radiation is of paramount importance in the field of radiation biology. Radiation, on one hand has helped life forms evolve and on the other, it manifests deleterious effects on life forms. Currently ionizing radiation is being used in a large number of therapeutic, diagnostic and industrial applications. In many instances where radiation is used for power generation, industrial/medical purposes or agricultural uses and food preservation, the personnel manning the radiation sources may be subjected to low level exposures. Exposures to high levels of radiation may occur due to accidents (like Chernobyl, Mayapuri in Delhi or the recent Fukushima catastrophe) or during “nuclear war”. Besides, radiation poses a major, un-resolvable risk for astronauts, especially for long-duration space flights. Radiation injury to normal tissues surrounding tumor is one of the major problems limiting the success of radiotherapy.

A significant part of the initial damage done to cells by ionizing radiation is due to the formation of reactive oxygen species (ROS), which reacts with almost all cellular components to induce oxidative damage (Cerutti, 1985; Repine et al., 1981; Yamaguchi et al., 1994). Free radicals can also initiate a variety of signal transduction pathways. These may either aid the cell in coping with the excess oxidative stress resulting from radiation or lead to cellular damage beyond the cell's repair capabilities (Ahmed and Li, 2008; Mikkelsen and Wardman, 2003).

For almost three decades, Walter Reed Army Institute of Research (WRAIR) supported an Anti-radiation Drug Development Program in which more than 4,000 compounds were synthesized and screened in mice (Sweeney, 1979). The most significant contribution of the WRAIR initiatives was the development of WR-2721 (S-2-(3-aminopropylamino) ethylphosphorothioic acid) as well as many related phosphorothioates, including WR-151327 (S-3-(3-methylaminopropylamino) propylphosphorothioic acid) and WR-3689 (S-2-(3-methylaminopropylamino) ethylphosphorothioic acid) (Brown et al., 1988; Sweeney, 1979). Of them, WR2721 (amifostine) which is considered the “gold standard” has already been approved for clinical use in conjunction with cisplatin chemotherapy and radiotherapy to treat
malignancies such as head and neck cancer. Despite its effectiveness, amifostine has not been accepted and approved as a radioprotector due to its toxicity. A number of drugs of both synthetic and biological origin have been tested for radioprotection in the last few decades (Foye, 1998; Nair et al, 2001; Weiss and Landauer, 2003; Weiss and Simic, 1988). Recently, nanoparticles are also being explored in the field of radioprotection (Ali et al, 2004; Daroczi et al, 2006; Deshpande et al, 2005; Rzigalinski, 2005; Schubert et al, 2006; Tarnuzzer et al, 2005; Trajkovic et al, 2007). Increased surface area and minute size of nanoparticles imply different spacing and arrangement of surface atoms resulting in unique interactions with cellular components, in a manner distinctly different from traditional pharmacology (Rzigalinski, 2005).

Alpha-lipoic acid (LA), C₈H₁₄O₂S₂, a disulfide derivative of octanoic acid, has been known to be a crucial prosthetic group of various cellular enzymatic complexes and characterized as an efficient antioxidant, for decades. It is a potential therapeutic agent in the treatment or prevention of different pathologies that may be related to an imbalance of the oxido-reductive cellular status (Juanita et al, 1998; Malińska and Winiarska, 2005; Packer et al, 1995).

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 (Searle, 2010). 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, 2010b; Wong et al, 2009). Previous studies from our lab have explored the radioprotecting properties of silver nanoparticle complexes of compounds such as glyzyrrhizic acid (Chandrasekharan et al, 2011b), gallic acid (Nair et al, 2010) and 6-palmitoyl ascorbic acid 2-glucoside (Chandrasekharan et al, 2011a).

Zinc, an essential nutrient, is the second most abundant trace element in human body. For many years, zinc salts have been used both topically and orally to treat burns as well as to enhance wound repair in men and animals (Gorodetsky et al,
Both organic and inorganic complexes of Zn have been reported to confer radioprotection under different in vitro and in vivo conditions (Ertekin et al., 2004; Floersheim et al., 1988; Floersheim and Floersheim, 1986; Mantena et al., 2008; Matsubara et al., 1986; Samuni et al., 1999; Sorenson et al., 1993)

Tempol is one of the most potent nitroxide that protects cells and tissues from the damaging effects of ROS (Krishna et al., 1998; Li et al., 2006). Several nitroxides including TPL have been shown to provide in vitro (Hahn et al., 1992b; Mitchell et al., 1991) and in vivo radioprotection (Hahn et al., 1998; Hahn et al., 1992a).

POLY-MVA is a commercially available dietary supplement containing the active ingredient, palladium- \( \alpha \)-lipoic acid (LAPd) complex. POLY-MVA was shown to regulate ischemic cell death and proved to be a potent neuroprotective agent for victims of transient ischemic attack, cardiac arrest, anesthetic accidents, or drowning (Antonawich et al., 2004). POLY-MVA could also protect the age-linked decline of mitochondrial enzymes and enhance the energy production of normal cell mitochondria (Sudheesh et al., 2009).

The present study focuses on evaluating the radioprotecting potential of the following agents – (i) nanoparticle complexes of Lipoic acid viz. Silver nanoparticle complex of LA (SNLA) and Zinc oxide nanoparticle complex of LA (ZNLA), (ii) Tempol and (iii) POLY-MVA. Their usefulness as adjuvants in tumor radiotherapy and chemotherapy is also explored.