Chapter 1
Introduction
The increasing application of gamma radiation for medical and industrial purposes is leading to an increase in the number of incidents with hazardous impacts on human beings. Apart from these, humans are also being exposed to ionizing radiation from background, accidental releases of radioisotopes, radiotherapy during cancer treatment, nuclear accidents (e.g., Chernobyl), during air and space travel. Recent nuclear power plant disaster at Fukusima has raised new safety issues and utility of nuclear power. Radiation can lead to skin burns, hair loss, birth defects, illness, cancer and death, depending on dose and duration of the exposure. Therefore, it is necessary to find a radioprotector which confer optimum protection against radiation. Ionizing radiation in interaction with living cells causes a variety of changes depending on exposed and absorbed dose, duration of exposure and interval after exposure and susceptibility of tissues (1). Radiation mediates it hazardous impacts on human directly by interacting with target molecules or by indirectly via the formation of free radicals such as hydrogen radical, hydroxyl radical, hydroperoxyl radical, hydrated electron, hydronium ion, superoxide anion, etc. These free radicals interact with different parts of the cell including cell membrane and different intracellular molecules like proteins and DNA. Gamma radiation can induce damage at three different functional units of the cell membrane such as the lipid bilayer, protein components and cytoskeleton part of the membrane and causes alteration in membrane structure with consequent loss of its barrier function that is vital for cell survival (2-4). Radiation induced toxic free radical causes single strand break, double strand break, oxidative damage to sugar and base residues, chromosomal aberration (1). Reactive oxygen species (ROS) is the key mediator of the inflammation as it is associated with the activation of redox sensitive transcriptional factor (NF-κB) (5). On activation, NF-κB regulates the expression of almost 400 different genes, which include enzymes (e.g., COX-2, iNOS etc.), cytokines (such as TNF-α, IL-1, IL-6, IL-8, and chemokines) etc. iNOS is responsible for prolonged production of larger amount of nitric oxide (NO). NO is a versatile molecule and signaling transducing second messenger. It is a potent pro-inflammatory agent too. Overproduction of NO can be autotoxic and contribute to tissue injury (6). In our very recent study it has also been reported that gamma radiation also causes inflammation (7). Therefore, it is of vital importance to search and validate a potent agents which can protect cells from radiation induced oxidative injury.

Several synthetic compounds like lipoic acid, deoxyspergualin, cysteine, cysteamine, 2-MPG, WR-2721, amifostine (S-2-(3-amino-propilamino) ethylphosphorothioic acid) were tested to be as good radioprotector (8-11). However their practical applications limited their use due to
the high systemic toxicity at their optimum protective dose. These consequences further emphasize the search for less or non-toxic compounds from biological origin. In recent times, the focus of research on plant and plant derived compounds include polyphenols such as hydroxybenzoic acids, hydroxycinnamic acids, anthocyanins, proanthocyanidins, flavonoids, stilbenes and lignans in terms of exploring the radioprotective activity has escalated owing to their natural basis (12). One such plant, *Moringa oleifera* Lam (Synonym *Moringa pterygosperma* Gaertn, family Moringaceae) is considered one of the world’s most useful trees among all the medicinal plants. *Moringa oleifera* leaf and its other parts are one of the most popular and easily affordable vegetables of Indian subcontinent. Leaves can be eaten fresh, cooked or stored as dried powder for many months without refrigeration. The plant is widely available as it propagates through both sexual and asexual means and its low demand for soil nutrients and water after being planted makes its production and management easy (13). Moringa shows radioprotective potential as the leaf extract protects bone marrow chromosomes against radiation induced damage (14). Leaf also possesses antioxidative (15), hepatoprotective (16, 17) activities. In addition, phenolic compounds from leaves of *Moringa oleifera* have been reported as anti cancer agents (18). Thus, *Moringa oleifera* leaf can be chosen as an excellent candidate for investigation as a radioprotector. For that reason, the present study has been undertaken to evaluate the role of crude leaf extract of *Moringa oleifera* on radiation hazards in Swiss albino mice.

Quercetin and epicatechin are the most abundant dietary flavonoids and these are widely available in large amounts in apple, onion, tea, red grapes, cherries, and citrus fruit (19-21). Previous studies have shown that these two phytocompounds effectively scavenge hydrogen peroxide and hydroxyl radical (22-24). Both of these two phytochemical also have shown lipid peroxidation inhibitory effect and thus prevent cell membrane damage (22, 25-28). In some previous studies it has also been found that quercetin and epicatechin ameliorate the gamma radiation induced DNA damage (29, 30). Anti-inflammatory and anti-tumor activities of these two phytocompounds also have been reported (31-35). Therefore, the objectives of this study were to investigate the effect of γ-radiation on whole mice in cellular and systemic level and to explore the protective mechanism of Moringa leaf extract and two flavonoids quercetin and epicatechin against radiation induced damage.