CHAPTER II

REVIEW OF LITERATURE
RADIATION

Gamma rays are the most dangerous form of radiation emitted by a nuclear explosion because of the difficulty in shielding them. This is because gamma rays have the shortest wavelength of all waves in the electromagnetic spectrum, and therefore have the greatest ability to penetrate through any gap, even a subatomic one, in what might otherwise be an effective shield.

Gamma-rays are not stopped by the skin. They can induce DNA alteration by interfering with the genetic material of the cell. DNA double-strand breaks are generally accepted to be the most biologically significant lesion by which ionizing radiation causes cancer and hereditary disease. A study done on Russian nuclear workers exposed to external whole-body gamma radiation at high cumulative doses shows the link between radiation exposure and death from leukemia, lung, liver, skeletal and other solid cancers. Alongside radiation, gamma-rays also produce thermal burn injuries and induce an immunosuppressive effect.

Increasing use of ionizing radiation for diagnostic as well as therapeutic purposes has drawn the attention of many radio-biologists towards the undesired side effects of such exposures. The
haematopoietic tissues due to their proliferate activity have received special attention.

Different cells of haematopoietic tissue show different sensitivity. Bauer (1940) reported that erythroblasts and haemocytoblasts are highly sensitive followed by myeloblast and finally megakaryocytes, but the most sensitive of all blood cells are the lymphocytes and their precursors.

After whole body exposure manifestations of injury to mammalian tissue are well reflected in peripheral blood (Rugh and Somogyi, 1968 Kumar et al. 1984 ; Shaheen and Hassan, 1991). Changes in blood cell counts are still considered (although imperfect indices) the most sensitive biological evidences of excessive acute exposure to both external and internal irradiation. This is because of high sensitivity of blood and blood forming tissue to ionic radiation.

Lorenz (1951) observed severe anemia in guinea pigs exposed to 200 RC one half of LD 50/30.

Krise et al. (1961) recorded a decline in white blood cells and lymphocyte counts in rats after whole body exposure to γ-rays.

Uma Devi and Kumar (1981) studied radiation induced changes in peripheral blood erythrocytes in male Swiss albino mice after whole body exposure to 250 R, 500 R, 1000 R of γ-radiation at a dose rate of 50 R/minute. After exposure to 250 R, the erythrocyte counts remained unchanged at 3 hour and then slowly decreased up to 3 days, after which the counts were slightly increased at 5 and 7
days, again decreased at 14 days. After exposure to 500R and 1000R the erythrocyte count continuously decreased up to the last autopsy time i.e. 14 days.

Kumar et al. (1982) injected male house rat (*Rattus-rattus*) with P-32 at the dose rate of 1.25 μCi/g body weight. The blood was collected at post-injection intervals of ½, 2, 4, 6 and 8 days and various haematological parameters were estimated. An initial decrease in leucocytes count and total plasma protein content (on day 2 and 4) were noted whereas erythrocyte count, haemoglobin percentage and haematocrit value decreased at later intervals only (on day 6 and 8).

A strong association between diagnostic x-rays (10-15 MGy) received by a foetus *in utero* and the development of the childhood leukemia before 10 years of age has been suggested (Upon 1979, 1987; Monson and Mac Mohan, 1984). Epidemiological studies have also shown an increase in the frequency of radiation induced carcinoma and leukemia in children after a prenatal exposure to diagnostic x-rays (Monson and Mac Mohan, 1984, Stewart, 1973; and Mole, 1979).

But the analysis of clinical observation is often difficult and the result in many cases have met with criticism (Neumeister and Wasser, 1985; Oppenheim, *et al.*, 1975; Mole, 1987). No systematic study has been reported on the late effects of diagnostic exposures at the different stages of intrauterine development in mice.
The effect of radiation on the peripheral blood of Swiss albino mice 70 days after exposure to 8.0, 9.0 and 10.0 Gy gamma rays was studied by Saini et al. (1985). Irradiation with lethal doses of γ-rays bring about a reduction in the blood levels of leucocytes, lymphocytes and erythrocytes on 70 days after exposures. The granulocyte percentage did not show any noticeable change after exposure to 8.0 and 9.0 Gy but it was significantly higher in 10.0 Gy irradiated animals as compared to that of the normal.

Male Swiss albino mice of six to eight weeks were exposed to 2.5, 5 and 10 Gy of Co$^{60}$ gamma radiations at the dose rate of 0.60 Gy/minute. Lymphocytes showed a drastic reduction in percentage at 12 hour, in all the groups reaching a minimum value at 72 hour. Thereafter counts increased gradually at all the three dose levels upto 10 days, followed by a second depletion on days 17. Once again an increase in the lymphocytes population was observed at 4 weeks, but the counts remained below normal.

Floersheim et al. (1988) recorded radiation-induced reduction in the haematocrit value and the number of thrombocytes, erythrocytes and leucocytes in mice after whole body gamma irradiation.

A group of pregnant mice was given priming injection of HIO of the activity 2.0 μci (74 KBq)/ml body water on 16.25 the day of gestation. Then they were maintained on tritiated drinking water of the activity 3/μci (111 KBq)/ml from the initiation through parturition till autopsy intervals. Minimums of 5 offspring were
sacrificed at 2, 3, 4 and 6 weeks of age. The total leucocyte and erythrocyte numbers and haemoglobin and hematocrit values were determined. The maximum decline (15%) in haemoglobin occurred on 2 weeks, which gradually recovered to 95% of the control by 6 weeks. Erythrocytes counts showed fluctuating values below 17 ± 2.5% of control upto 4 weeks of age which also recovered to 93.90% of the control by 6 weeks of age. Leucocyte counts showed the highest depletion among all the parameters (by 45% on 2nd week to 15% at 6th week). (Heada and Bhatia, 1986). The differential counts of leucocytes showed statistically significant rise in eosinophils on 3 & 4 week and neutrophils by 90% of control on 2nd week. Concomitantly a sharp rise in abnormal and degenerating cells from 3 weeks onward upto 6 weeks of age has been noticed whereas lymphocytes were throughout depleted from 33.78% on 2nd to 10.25% on 6th week. MCV in noticed significantly lower on 2 & 3 weeks of age, which were higher values with a maximum coinciding with MCV on 4th week of age. MCHC value after on initial increase on 2nd week of age comes down to control value and remained around upto last interval studied.

Hande et al. (1990) exposed pregnant mice to single dose of diagnostic x-rays (9MGY) at 3.5 day post coitus (d.p.c.). 6.5 d.p.c. or 11.5 d.p.c. Peripheral blood changes were observed at 6 weeks and 3, 6 and 12 months of age in the offspring by estimating total RBC, WBC and haemoglobin. Haemoglobin level and RBC count at 3 months in the 6.5 d.p.c. exposed group and at 6 months in the 3.5 d.p.c. group, whereas a significant increase in the total leucocytes
was observed at 12 months in the animals exposed on the 11.5 of intrauterine life. Differential leucocytes count revealed that a change in the number of lymphocytes was responsible for the increase or decrease in the total leucocyte count. These findings could be significant in interpreting the excess leukemia cases reported in epidemiological studies in the exposed populations.

Prakash et al. (1990) exposed pregnant mice to single dose of diagnostic x-rays at 3.5 day post-coitus, 6.5 d.p.c. or 11.5 d.p.c. and noticed the various haematological changes at 6 weeks and 3, 6 and 12 months of age in the offspring. Haemoglobin level and RBC counts did not show any change in any of the groups. There was a reduction in the total W.B.C. count at 6 months in the animals exposed on day 11.5 of intrauterine life.

Exposure of BALB /C mice to different doses of Co\textsuperscript{60} gamma radiation induces dose-dependent increases in the frequency of micronucleated polychromatic erythrocytes (MPCE) and micronucleated normochromatic erythrocytes (MNCE) in the bone marrow. The polychromatic / normochromatic erythrocyte ratio (P/N) decreased gradually after exposure to various doses of gamma radiation. The dose-response relationship was linear-quadratic for MPCE, MNCE and P/N ratio for all groups of animals (Jacob and Jagetia, 1992; Ganapathi and jagetia, 1995).

Daga et al. (1995) noticed the alteration in some haematological parameters like haemoglobin level, haematocrit value and erythrocyte sedimentation rate (ESR) in male Swiss albino
mice after single whole body exposure to two different sub-lethal doses (1.20 or 3.60 Gy) of Co\textsuperscript{60} \(\gamma\)-radiation. At 1.2 Gy, haemoglobin exhibited a decline till day 5 and then started to elevate but remained below normal at last autopsy interval. Haematocrit value decreased till day 7, perpetually in both the groups. In 3.60 Gy treated animals both haemoglobin and haematocrit value decreased till day 14. The ESR level increased till day 7 and 14 in 1.20 and 3.60 Gy control animal respectively.

In another experiment with similar doses to male Swiss albino mice Daga \textit{et al.} (1995) recorded a decrease in total leucocytes count (TLC) at 1.20 Gy dose till day 1 ; whereas in higher dose until day 5 with a sharpness in first 24 hour. Lymphocytes also declined sharply in both the radiation dose up to day 1, after that showed a recovery towards normal count on day 28. The behaviour of neutrophils was reciprocal to that of lymphocytes as they showed a rise till day 1 followed by a gradual decline up to day 5 leading to a second peak on day 14 in exposed animal with both the radiation doses.

Lim \textit{et al.} (1977) evaluated the relationship between radiation dose to bone marrow and subsequent changes in peripheral blood cell counts.

Nabila \textit{et al.}(2009) studied effect of gamma radiation on some biophysical properties of red blood cell membrane from three different but correlated properties electrical, mechanical and chemical, and to derive useful parameters for the evaluation of radiation effects. AC conductivity of cell suspension was measured
in the frequency range 40 kHz to 5 MHz, the osmotic fragility of the membrane and solubilization of the membrane by detergent were also measured. Adult male rats were exposed to 1, 2.5, 3.5, 5, 7 and 9 Gy gamma radiation from Cs137 source. The results showed decrease in the AC conductivity, average osmotic fragility and average membrane solubilization. The effect of radiation on the red blood cell membrane was discussed.

**CADMIUM**

Decalcification of bones was a prominent feature of “Itai-Itai” disease in the Jintzu River Basin in Japan and Shipham, a zinc-mining town in England. “Itai-Itai” disease was first diagnosed as vitamin D resistant osteomalacia. Hagino and Yoshilka (1961), Ishizaki (1965), Tsuchiya (1978), have reported this disease as a manifestation of excessive intake of cadmium. Studies on health surveys of cadmium polluted areas also revealed that multiple nutritional factors such as deficiency of vitamin D, low intake of calcium and generalized malnutrition problem of high intake of cadmium in rice, are the cause of “Itai-Itai” disease and osteomalacia (Murata et al., 1970; Friberg et al., 1974; Shigematsu et al., 1979).

Kazantzis et al. (1963) investigated pulmonary emphysema in cadmium pigment workers. Cross et al.(1970) have observed inhibition of Na⁺, K⁺, Mg⁺, ATPase system and endogenous respiration of alveolar macrophage cells. Pulmonary dysfunction due to higher intake of cadmium was observed by Friberg et al. (1974).
Loose et al. (1978) noted the influence of cadmium on the phagocyte and microbicidal activity of marine peritoneal pulmonary macrophages. Several pathological and biochemical changes in lungs of rat due to inhalation of cadmium was recorded by Hart (1986). Cadmium in cigarette smoke was found hazardous to lungs (Bache et al., 1986).

High cadmium concentration in the exposed animals induces haematological changes. Axelsson and Piscator (1966) have reported reduced plasma haemoglobin level induced by the higher administration of cadmium. Stowe et al. (1972) recorded a gradual increase in total serum proteins after three months of oral exposure to cadmium. Male rats treated with cadmium chloride showed higher SGOT and SGPT activity (Chaptwala et al., 1980). Single exposure of cadmium to mice suppresses the antigen antibody response (Fujimake et al., 1982). Weigel et al. (1984) studied the effect of low doses of dietary cadmium oxide on the haematological parameters. They reported that the haematocrit and haemoglobin remained unchanged and the number of RBC slightly increased. Donaldson (1985) noted effect of cadmium on fatty acid composition of blood serum and erythrocyte membrane of chicks. Hilmy et al. (1985) observed the toxic effects of cadmium on serum proteins and some key enzymes. Excess supply of cadmium impairs haemoglobin percentage and erythrocytes followed with decrease of body weight in fishes (Gill and Pant, 1986). Kumari and Banerjee (1986) noticed no significant change in shape, length, breadth and surface area of erythrocytes, but observed a change in the shape of
nucleus from round to oval. TEC, Hb content and PCV showed significant decrease whereas ESR and MCV increased significantly in cadmium chloride treated fish. Leucocytes are found to be hypersensitive to cadmium. Excess supply of cadmium to rats changes the properties of blood cell membrane and increased blood density (Itoh and Ozasa, 1986). In rats it has been demonstrated that intoxication by cadmium can hinder the resorption of iron, resulting is an iron deficiency anaemia (Huebers et al., 1987). Banerjee and Verma (1987) in cadmium chloride treated fish reported that large and small lymphocytes show significant increase and decrease respectively along with slight decrease in monocytes and neutrophils but show no marked deviation in basophil percentage. TLC increases significantly. Prakash et al. (1988c) observed a decrease in R.B.C. and W.B.C. count, haemoglobin percentage and increased level of SGOT and SGPT in blood of rat induced by the manifestation of cadmium toxicity. Gupta et al. (1989) recorded significant increase in α-tocopherol level in the plasma of weaned rats treated intraperitoneally daily for 30 days with various metals. Simultaneous administration of vitamin E reduces the cadmium induced biochemical alterations and the accumulation of cadmium in blood (Tandon et al., 1991). Mukherjee and Sinha (1993) after 2 weeks of treatment of cadmium recorded a marked decrease in haemoglobin, haematocrit value, total number of RBC, plasma protein and glycogen content of liver and muscle along with increased values of mean corpuscular volume, mean corpuscular haemoglobin and blood glucose. Gupta et al. (1994) noted inhibition of δ-ALAD activity of blood on exposure to lead and cadmium in isolation and
combination; the extent of which increases with duration of exposure. Adiga and Jagetia (1994) reported cadmium chloride induced dose dependent increase in the frequency of micronucleated polychromatic erythrocytes (MPCE) and micronucleated normochromatic erythrocyte (MNCE). The polychromatic erythrocytes (PCF)/ normochromatic erythrocytes (NCE)- ratio declined with the increase in cadmium chloride dose and this depletion was dose dependent. Bala et al. (1994) recorded a significant decline in total RBC count of blood in adult *Channa punctatus* exposed to sublethal concentration of cadmium chloride, lead nitrate and zinc sulphate. Sastry and Gupta (1994) reported decline in haemoglobin concentration, packed cell volume, mean cell haemoglobin concentration and total erythrocyte count and increase in mean cells volume, mean cell haemoglobin in the blood of *Channa punctatus* on exposure to sub lethal concentration of cadmium and dimethoate alone as well as in combination. A significant decline in TEC, haemoglobin percentage and serum protein level and increase in blood glucose and plasma cholesterol of fresh water fish, *Channa punctatus* on exposure to sublethal concentration of cadmium chloride was reported by Patil and Dhane (1996), Dhane and Patil (1997) recorded a decrease in blood glucose level when the hepatic glycogen was low.

Although liver acts as detoxifying agent in animal body but effects of cadmium on liver have been reported. Dalvi and Robbins (1978) performed comparative studies on the effect of cadmium, lead and selenium on hepatic microsomal monoxygenase enzyme
and glutathione level in mice. Dubale and Shah (1979) reported lesions in liver and kidney induced by cadmium nitrate toxicity. The damage in kidney was slower than the liver. Exposure of *Channa punctatus* to different concentrations of cadmium nitrate initially showed a gradual depletion in the contents of glycogen and protein and a rise in cholesterol in liver (Dubale and Shah, 1980). Chaptwala *et al.* (1982) observed a significant increase in serum glucose, serum protein, SGOT, SGPT, Glucose-6-Phosphatase, Fructose-1,6-di phosphatase, phosphoenol pyruvate carboxykinase and pyruvate carboxylase in liver and kidney of male Sprague-Dawley rats injected intraperitoneally with cadmium. Dudley *et al.* (1984) recorded time course of cadmium induced ultra-structural changes in rat liver. Higher dose of cadmium to rats seems to change the histology of liver (Peter and Helmut, 1984). Weigel *et al.* (1984) reported increased SGOT and SGPT activities, indicating disturbed hepatic functions, in male Wistar rats exposed to cadmium oxide. Cadmium chloride induced decrease in glycogen content and increase in the collagen content in liver of rats was shown by Rana *et al.* (1985).

Mumtaz (1986) reported that higher concentration of cadmium suppresses the microsomal drug metabolizing enzyme system in liver of guinea pig. Muller (1986) observed mitochondrial dysfunction in liver of rat induced by cadmium toxicity. Nath (1986) reported hepatic lesions as a manifestation of cadmium intoxication. Rat exposed to cadmium chloride showed a decreased enzyme activity in liver (Prakash *et al.*, 1987, 1988a). Decreased
carbohydrate and proteins followed with fatty liver were observed after cadmium administration (Prakash et al., 1988b). Gupta et al. (1989) recorded a significant decrease in α-tocopherol level in the liver of weaned rats treated intraperitoneally with various metals. Saleem et al. (1989) investigated that the level of marker enzymes of hepatotoxicity-GPT and GOT decreased and serum level of GPT and GOT increased significantly in protein malnourished rats by chronic cadmium exposure. Sastry and Shukla (1990) reported decrease in rate of oxygen consumption, total plasma proteins, the level of glycogen, lactic acid, pyruvic acid and total proteins and increase in glutamate oxaloacetate transaminase and glutamate pyruvate transaminase activities in liver of cadmium exposed *Channa punctatus*. Swamalatha and Ramamurthi (1993) reported dissary of hepatic cords, cloudy swelling of cells, vascular degeneration, engrosement of central and peripheral blood vessels on necrosis induced by cadmium given orally to albino rats. Glutamate dehydrogenase activity was inhibited by chromium and cadmium alone while increases with the combined effect of the two metals (Sastry and Gupta, 1993). Sastry et al. (1997) reported increase in the activities of LDH, MDH, GDH, XO, GPT and GOT but activities of SDH and PDH decreased in liver of *Channa punctatus* exposed to cadmium and copper individually while on the combination of the two heavy metals, the level of lactic acid decreased and the level of pyruvic acid increased.

Excessive intake of cadmium induces alteration in histopathology, histochemistry and biochemistry of renal tissues.
Nomiyama et al. (1973) reported the loss of body weight and increased urinary excretion of protein, alkaline phosphatase and acid phosphatase to be early warning signs suggestive of renal injuries due to cadmium exposure. Bhardwaj (1980) reported tubular necrosis, glomerulonephritis, reticulocytosis, and inflammation of collecting tubules and epithelia damage of PCT and DCT due to cadmium toxicity. Rana et al. (1980) and Kumar et al. (1980) observed the effects of cadmium on carbohydrates, proteins lipids in the kidney of rats. Toxic effects of cadmium on kidney of mice and rat was studied by Friberg (1984). Morsett et al. (1984) recorded histochemical change in protein disulphide bonds in liver and kidney of rat after chronic administration. In 1984, Aughey et al. recorded histopathological changes in the kidney of rat as a manifestation of higher cadmium intake. In a similar experiment Diamond et al. (1986) observed kidney dysfunction. In 1987, Jana and Bandhopadhyaya recorded a decrease in protein and RNA content and dry weight and increase in free amino acid content and activities of protease and ribonuclease in liver and kidney. Cadmium acetate inhibits the activity of superoxide dismutase, to increase the endogenous level of lipid peroxides and lipid peroxidation in the liver and kidney (Hussain et al., 1987). Jeelani et al. (1988) registered fall in the enzyme activity in kidney of three fish species i.e. Labeo rohita, Clarias batrachus and Channa punctatus. Simultaneous administration of vitamin E reduces the cadmium induced biochemical alterations viz. decreased activity of hepatic and renal glutamic oxaloacetic and glutamic pyruvic transaminases and alkaline phosphatase accompanied by increase in the level of

Cadmium toxicity directly affects central nervous system. Cadmium inhibits neuromuscular transmission in rat (Forshaw, 1977). Arvidson (1980) observed cadmium-induced lesions in peripheral nervous system in mice. Accumulation of cadmium in the brain of rat was recorded by Clark et al. (1985). The administration of cadmium disturbs the lipid composition in rat brain (Gulati et al., 1986). Gabbiani et al. (1967) observed toxic effect of cadmium chloride on sensory ganglia. Jeelani et al. (1988) recorded fall in hexokinase activity in brain after 5 hours of cadmium chloride exposure. Shukla et al. (1988) investigated that the simultaneous administration of vitamin E prevents cadmium-induced changes in glutathione (GSH) and oxidized glutathione (GSSG) levels and in the GSH / GSSG ratio, while the cerebellar GSH remained lowered. Gupta et al. (1989) noticed a significant decrease in dopamine content in corpus striatum, cerebral cortex and hippocampus regions while significant increases were found in hypothalamus and cerebellum region. Nor epinephrine increases in corpus striatum, cerebellum, cerebral cortex and hypothalamus regions where as diseases in pons medulla epinephrine was found to decrease in corpus striatum, cerebellum, cerebral cortex and hippocampus
regions and increased in pons medulla. 5-Hydroxytryptamine and its metabolites 5-HIAA increased in almost all the regions except cerebral cortex due to cadmium toxicity. Gupta et al. (1989) recorded a significant decrease in α-tocopherol level in the brain of weaned rats treated intraperitoneally with various metals.

Ingested cadmium is reported to cause gastrointestinal irritation. Gunn et al. (1963) observed cadmium induced intestinal tumors. Cadmium poisoning induces catarhal and ulcerative gastroenteritis (Friberg et al., 1974). Effects of cadmium in vivo and in vitro were found on intestinal brush border AlPase and ATPase (Sugawara and Sugawara, 1975). Sastry and Gupta (1979) reported necrosis and degeneration in villi of intestine followed by pyknotic nuclei in fish exposed to cadmium chloride. Cadmium acetate induces degenerative changes in the caecal cells of Gigantocotyle species intestine (Gupta et al., 1989). Sastry et al. (1993) reported that cadmium or lead alone reduces the rate of transport of glucose and xylose but the combination of both the metals inhibits Na⁺, K⁺ and ATPase activity in the intestine of albino rats. Sharma and Singhal (1993) pointed out that cadmium decreases the digestive efficiency by inhibiting the activity of number of enzyme. Vincent and Ambrose (1994) showed a significant decrease in enzyme activity partially in gill and intestine of Indian major carp, Catla catla exposed to sub lethal concentration of cadmium.

Parizek (1957) was first to diagnose the effects of cadmium exposure on the male reproductive system after single injection of cadmium salt, it was found to develop necrosis resulting in
permanent loss of fertility. Testes of rat poisoned with cadmium salt loose their capacity to manufacture testosterone (Favino et al., 1966). Mouse fed on supplementary diet of cadmium showed changes in adenylate energy and total adenine nucleotide concentrations in testes (Itoh, 1985). Chauhan and Agrawal (1989) observed tubular deformation, disorganization of germ cell layers, their exfoliation in the tubular lumen and decrease in weight of testes, seminiferous tubules diameter, sertoli cells, gametogenic count and nuclear diameter in the testes of male albino rats administered subcutaneously by cadmium chloride. Higher administration of cadmium checks the gonadal development and fertility in mice (Tom and Liu, 1985).

Marked hyperaemia of the ovary and atresia of follicles after administration of cadmium were recorded by Kar and Das (1960). Kaul and Ramaswami (1970) studied the effect of cadmium chloride on the ovary of the Indian desert gerbil. Banerjee and Lal (1989) reported retardation of oocyte maturation and atresia of oocyte and depletion in the ovarian triglycerides concentration due to cadmium chloride and lead nitrate in *Channa punctatus*. Enzymatological and histochemical changes in testes and ovary were observed by several researchers (Nordberg, 1971, Taylor et al., 1973 and Passai et al., 1985). Nandini and Agrawal (1988) reported cadmium-induced lesions in ovary and testes of albino rats. Toxicant mixture of cadmium, DDVP, Parnol-J and N-heptane reduces fish production, fecundity and maturity index of both male and female fish and survival rate (Ghatak and Konar, 1993).
Inhalation of cadmium causes cardiovascular disease. A number of epidemiological studies showed that cadmium is linked to human hypertension and cardiovascular disease (Whanger, 1979 and Perry et al., 1979). Germano et al. (1984) reported that administration of cadmium to rats disturbs the heart beat rate. Chronical cadmium exposure induces necrosis and cardiac cell inflammation in rat and disturbance in the mechanism of cardiovascular regulation in male rabbit (Boscolo and Carmignani, 1986). Kagamimori et al. (1986) diagnosed depressed cardiovascular function in females due to excess cadmium administration.

Potential carcinogenic effects of cadmium in experimental animals and man have been noted by Malcolm (1972). Frost (1977), Frust (1978) and Elinder et al. (1985) reported carcinogenic effect of cadmium. Mortality and cancer morbidity among cadmium exposed workers have been noted by Kjellstrom et al. (1979). Takenaka et al. (1983) reported carcinogenicity of cadmium chloride aerosol in rats. Carcinogenic effect on prostrate gland due to higher concentration of cadmium was reported by Hoffman et al. (1985). In 1986, Kazantzis and Lam noted great mortality in cadmium workers due to cancer.

Cadmium induces fusion and disruption of ciliated structure in the free border of epithelium, rupture of the receptor and supporting cells, damage of microvilli on the non-sensory epithelium and fragmentation of micro ridges of the stratified epithelium cells in the olfactory epithelium (Chakrabarti et al., 1973). Cadmium stimulates DNA synthesis and exerts adverse effects of RNA (Rana et al., 1980). Narssen (1993) reported instant death of Blepharisma
intermedium due to lethal toxicity of cadmium chloride. In 1996, Kandu and Saha reported karyodistortive effect of CdCl₂ in male germ line cells. The chromosome aberrations were mainly breaks, gaps, constrictions, pulverization and polyploidy.

Cadmium is eliminated from the body thorough the renal glomeruli causing histological and biochemical alterations. Excretion of cadmium from rat kidney was recorded by the interactions of DTPA and DMSA by Eybl et al. (1984), Cystein was reported to protect liver injury induced by orally administered cadmium (Prakash, 1985). Maitani et al. (1986) reported cystein as antidote for cadmium. Recently, methionine and penicillamine were noted to reverse histological, biochemical and histochemical lesions induced by cadmium in liver and kidney of albino rat (Prakash et al., 1987, 1988b, 1988c).

The numbers of reports concerning chemical toxicology of metals, which are released in the environment by natural as well as anthropogenic sources, have been increasing constantly. Recently, it is hypothesized that these metals exert their toxic effect by damaging biological defenses which exist in the body to serve as protective mechanisms against exogenous toxins.

**Combined effect of CdCl₂ and Radiation on blood:**

Interaction of metals with other agents is an important aspect as both can interact in a “synergistic” or “additive synergistic” manner and further aggravating the situation. The combined effect of chemical and radiation have mostly been studied on inborn babies
because of their high sensitivity to those toxicants. The general aspect of the interaction between radiations and chemicals during prenatal development were summarized in the UNSCEAR report (1982) and later reviewed by Streffer (1984) on the interaction between ionizing radiation lead, actoncysin -D, phenols, sodium nitrate and caffeine, etc.

Muller et al. (1982) carried out in vitro studies on individual and combined exposure of x-rays and cadmium sulphate, Cadmium floride on mouse embryos. The effect of cadmium and radiation on foetuses.

The effect of combined treatment of Cd and γ-radiation on DNA damage and repair was studied in lymphoid tissues of mice using single cell gel assay (Privezentsev et al., 1996). He observed that single O.P. injection of CdCl₂ (1 mg Cd/kg body wt.), 2 hour prior to irradiation resulted in increasing of DNA lesions in peripheral blood lymphocytes when compared to non-injected animals.

Introduction of CdCl₂ (0.75 mg / kg Ca²⁺), in combination with γ-irradiation of mice increases the level of metallothioneines (MTS) in the bone marrow of mice. The maximum effect was observed in 24-30 hour after the performance. The effect of single subcutaneous injection of CdCl₂ on haemopoiesis in normal (non-irradiated or irradiated) mice was studied by Fedorocko et al. (1996). Cadmium doses used ranged from 1-8 mg/ Kg body wt. 24 hour after cadmium treatment (doses from 3 to 8 mg/kg) there was no
significant changes in bone marrow cellularity and granulocyte macrophage progenitor cell (GM-CFC), number per femur in non-irradiated female ICR mice.

Similarly during the 30 day post-injection period bone marrow cellularity and marrow GM-CFC number in mice treated with a cadmium dose of 5 mg/kg were not significantly different from the control values. Cadmium significantly reduced the lethal effect of γ-rays. In addition, increasing the doses of cadmium administered 24 hour prior to sub lethal irradiation increased the number of endogenous haemopoietic stem cells in a concentration-dependent manner.

Privezentsev (1997) using micronucleus test showed that CdCl₂ in drinking water dose not induce cytogenetic damages in mouse bone marrow cells and dose not affect the yield of micronuclei (Mn) after chronic γ-irradiation (1 Gy), whereas CdCl₂ injection leads to an increase in the number of micronuclei. At the same time, both acute and chronic Cd⁴⁺ treatments decrease the no. of MN induced by acute irradiation.

Daga et al. (1998) exposed mice to sub lethal dose of 1.20 Gy CO⁰⁰ γ-radiations and observed that haemoglobin and haematocrit value declined till day 5 and could not regain to normal level till day 28. While erythrocyte sedimentation rate (ESR) value was evaluated up to day 7 post-irradiation and then started to decline but did not reach to normal even till day 28. In mice treated with methyl mercuric chloride, the Hb level and haematocrit diminished while
ESR elevated up to day 7 without regaining the normal levels even till the end of experimentation. In combined treatment group, the haemoglobin percentage and haematocrit values were significantly different than MMC or irradiation alone group showing a “synergistic” effect of these two teratogens.

Jaimala et al. (2001) recorded mortality, body weight, organ weight, haematocrit value and haemoglobin percentage in irradiated Swiss albino mice with or without cadmium chloride treatment killed at 1, 2, 3, 7, 10, 14, 28 days after treatment. It was observed that the given dose of CdCl₂ affects body functions of the animals but weight of almost all the organ was affected is not sufficient to cause any mortality in the CdCl₂ treated animal.

**Chemical protection:**

**Cadmium Protection:**

For the protection of living organism against cadmium-induced damage to various organs, various chemical agents are being investigated by many scientists. They minimize or prevent the toxic effect of metals are known as chemical protectors.

Parizek (1957) demonstrated zinc as to protect or reverse the cadmium induced toxic manifestations in animals. Further, pretreatment with zinc completely prevented the biochemical and functional damage if spermatogenic cells by cadmium. The administration of higher doses of zinc may recapture its own sites by displacing cadmium there by protecting tissue from damage.
Kar et al. (1960) investigated the protective effect of selenium against cadmium-induced toxicity. The protective action of selenium may be due to the formation of a temporary complex with cadmium (Gunn et al., 1966). Merali and Singhal (1975) reported that both selenium and zinc are effective in protecting animal against cadmium-induced alterations in glucose tolerance and insuline release response to a glucose load.

McCay et al. (1979) discovered antioxidant, vitamin E to inhibit lipid peroxidation processes and protect the biological tissues from the oxidative damage. High levels of vitamin E has been reported to suppress lipid peroxidation (Korbrust and Mavis, 1980) and the chronic vitamin E deficiency in experimental animals was found to increase the accumulation of lipofuscin in nervous tissue (Sulkin and Srivanij, 1970; Nandy, 1971). Shukla et al. (1988) investigated that the simultaneous administration of vitamin E and cadmium prevented cadmium-induced change in GSH and GSSG levels and in the GSH/GSSG ratio in different brain region of rat.

Maitani et al. (1986) reported cystein as antidote for cadmium. Cystein was recorded to protect liver injury induced by orally administered cadmium.

Das and Kaviraj (1992) studied the impact of chelating agent EDTA on the accumulation of cadmium in liver, kidney and intestine. It was observed that when EDTA was administered with cadmium salt there was no accumulation in liver while kidney and intestine showed a sufficient decrease.
Radiation Protection:

The radiation response of any tissue depends upon the chemical nature of the target material and its environment. The radiation response can be reduced by modifying the environment of the target material chemically (chemical radioprotection).

Thus, chemical protectors decrease the magnitude of such diverse responses like inactivation of enzymes, chromosomal aberration, gene mutation, acute radiation syndrome in mammals, erythema, epilation and delayed effects (Sterility and carcinogenesis). However, this statement should not be construed as meaning that every single protector shows activity in any organism tested or protected against any type of damage. Some protectors are active in some organisms but not in others (Arena, 1971).

Chemical radiation protection has a history of barely 50 years. The property of sulphur compounds to protect against damage in complex chemical systems was recognized in the early 1940’s. However, active research on the mammalian protection started about a decade later. The first demonstration that certain chemicals can reduce the X-ray induced damage was made by Dale (1942) in enzyme systems. But the first report on *in vivo* protection in mammals came in 1949, when Patt *et al.* published a study in which they observed that prior administration of cysteine, a naturally occurring amino acid, increased the survival of lethally irradiated rats and mice. This was followed by the discovery of more potent chemicals than cysteine in protecting against radiation induced...
mortality in laboratory mammals. Several compounds of different pharmacological activities were shown to have radioprotective property (Thomson, 1962), but none of them proved to be as good as the aminothiol chemicals, included under the cysteine-cysteamine group (Bacq and Alexander, 1961).

The adult Swiss albino mice were treated with 5.0 μ Ci/gm Body weight of tritiated water (HTO) in the presence (experimental group) and absence (control group) of 2-MPG by Gupta et al. (1979). The liver was studied at 1, 3, 7 and 14 days after the HTO treatment. The percentage of binucleate cells and abnormal hepatic nuclei were also calculated. In the control animals the hepatic damage was pronounced and the recovery was delayed as compared with experimental animals and the increase in percentage of binucleate cells and abnormal nuclei was also more remarkable in this group. Protection was pronounced at the early intervals but at later autopsy intervals the drug effect was less obvious as compared to the externally irradiated animals. They attributed this finding to the persistent irradiation source in the body even after the protector has been eliminated by excretion.

Adult Swiss albino mice were treated with P-32 (2.5 μ Ci/gm body weight) in the presence and absence of the drug MPG. A significant protective effect of the drug was noticed in the liver against the radiation induced increase in total proteins, acid phosphatase activity, glycogen and cholesterol contents. The protective effect noted for these parameters was well in agreement with the histopathological studies, in which almost normal structure
was attained on the 7th day post-treatment as against the 14th day in the non-drug treated animals (Bhartiya and Khan, 1981).

WR-2721 has been reported to selectively protect normal tissues and to concentrate in the liver. Utley et al. (1976a) observed an increased uptake of $S^{35}$, WR-2721 by liver and suggested the probability of its protection by this drug against.

Protection against later radiation injury of skin by WR-2721 has been observed by Lowy and Baker (1972). In Monogrel dogs Utley et al. (1977) found that following irradiation, the DRF of skin and oral mucosal structure was 1.7 and the effect of 25 Gy in WR-2721 treated animals and of 15-Gy in non drug treated animals was comparable. Utley et al. (1981) further studied the protection of later radiation damage by the drug in skin, muscles and vascular tissues of rats and found that the late effects were markedly diminished in the drug protected animals. Acute skin reaction graded over a period of six months was decreased by the drug with a DMF of 1.5. Radiation atrophy of skeletal muscles was significantly reduced as measured by changes in cross skeletal diameter of muscle fiber (p<0.05).

Injection of WR-2721 before radiation exposure significantly increased the radiation resistance of both the skin and bone marrow of mice, without altering the radio sensitivity of the solid tumor they bore (Yuhas and Storer, 1969b). This observation has been confirmed and expanded by Yuhas et al. (1980) and Yuhas (1981).

Meena (2006) also studied modulatory influence of polybion against 5.0 Gy gamma radiations and cadmium induced
haematological changes in the Swiss albino mice. He observed a decrease in the values of RBC, WBC, Hb, PCV and MCV in all the groups. Whereas the value of MCH and MCHC were increased in all the groups. These changes were less severe in the polybion treated groups showing protective efficacy of the drug.

Purohit et al. (2007) studied protective effect of polybion against radiation (5.0 Gy) and cadmium induced histopathological changes in the liver of Swiss albino mice. The changes observed were distortion of hepatic architecture, intracellular oedema, narrower sinusoids, cytoplasmic degranulation, vacuolation, hyperaemia, pycnotic and crenated nuclei. After combined treatment of radiation and cadmium chloride synergistic effects were observed. The liver of polybion treated animals exhibited less severe damage as compared to non-drug treated animals at all the corresponding intervals.

Agarwal (2010) studied protective effect of Aloe vera against radiation and cadmium induced haematological changes in the Swiss albino mice. She observed changes in the value of RBC, WBC, Hb, PCV, MCH, MCHC, TLC, SGPT and SGOT. All these parameters exhibited modulations in the form of increase or decrease following treatment of cadmium chloride and radiation exposure independently as well as in combination with or without Aloe vera. The values of RBC, WBC, Hb, PCV and MCV were found to decrease in all the groups as compared to normal group. The values of MCH and MCHC increased in all the groups as compared with normal group after 1, 2, 4, 7, 14 and 28 days of post-treatment intervals. The
values of SGOT and SGPT elevated up to day-14 in the non drug treated groups and day-7 in the *Aloe vera* treated groups, thereafter a fall in the value was seen up to day-28. After combined treatment of radiation and cadmium the changes were more severe and there was late manifestation of recovery. In the *Aloe vera* treated animals the changes were less severe and an early recovery was also observed.

**Liv. 52:**

Vyas (1960) concluded that Liv.52 is a well tolerated non-toxic, efficacious drug in cirrhosis of the liver in children especially, where it is in the early and intermediate stages.

Long term experimental study has established the protective effect of Liv. 52 against CCl₄ induced poisoning on liver in rats and rabbits. Both in rats as well as in rabbits Liv.52 could prolong the survival time considerably (Karandikar *et al.* 1963).

Liv.52 when administered to healthy guinea pigs, rats and mice showed a definite growth promoting effect which is due to increased food consumption as well as more efficient food utilization (Srinivasan and Balwari, 1968)

Indirabai *et al.* (1970) stated that Liv.52 stimulates appetite and promotes a feeling of physical and mental well beings. It is a powerful hepatic stimulant which increases the functional efficiency of the liver considerably (Arora, 1969).
Since the liver plays an important modifying or complicating role in energy illness or diseases. Liv.52 which protects, corrects, and stimulates liver function can be added with advantage to specific therapy in dermatological disorders by enhancing liver function, promoting metabolism and it helps to shorten the period of therapy (Behl, 1972).

Liv.52 is a suitable agent in a most debilitating disease like malignancy. Limitations and untoward side effects associated with steroids and hormones are not present with Liv.52 therapy. Incidentally the hepatotoxicity associated with the chemotheraphy (Oncolytic drug) is also sufficiently controlled (Gajraj and Munuswamy, 1972).

Liv.52 has a similar action in producing Nitrogen balance as the anabolic steroids. However, it is safe, non-toxic and has multiple actions, like hepatic stimulant, choleric, stomachic anabolic, etiotropic and encourages normal growth in children. It appears that Liv.52 has a definite and well established place in the therapy of anorexia and malnutrition (Dave et al., 1973)

Many hepatic enzyme levels have been shown to be affected by Liv.52 administration in rats (Saxena and Garg, 1973). A significant enhancement in the -SH levels in animals treated with Liv.52 has also been observed (Kumari, 1989).

Liv.52 seems to be a useful drug for therapy of acute viral hepatitis. There was rapid amelioration of clinical symptoms and signs, through total period of recovery was not materially affected.
The response seems to be very similar to that of steroids but without the latter's effect's weight loss is also minimum with Liv.52 (Sama et al., 1976).

An attempt has been made by Subbarao and Gupta (1978) to re-examine the hepatoprotective action of Liv.52 in albino rats against CCl₄ induced hepatotoxicity by assessing and studying certain biochemically altered parameters. Treatment of animals with Liv.52, 5-days prior to the challenge prevents this radiation in ribosomal protein and RNA seen after the administration of CCl₄ alone. Liv.52 by itself does not cause an alteration in these parameters but it significantly protects against the damaging action of CCl₄. In this study CCl₄ decreased the hepatic RNA as well as microsomal protein. It was observed that prior and subsequent administration of Liv.52 prevents the changes caused by CCl₄ but Liv.52 alone does not cause any significant change in the liver proteins and nucleic acid.

Kulkarni (1978) concluded that Liv.52 has a definite place in the treatment of malignant disease as are adjuvant to radiation therapy and cytotoxic drugs as the hepatotoxicity is evidently less.

Liv.52 has some protective action against alcohol and contraceptives induced liver damage (Subbarao, 1974 and Khuteta, 1978).

It could also be emphasized that Liv.52 aided quicker regeneration of the hepatic parenchyma and also it's stimulating
action markedly increased the functional efficiency of the liver (Subbarao and Gupta, 1976)

Liv.52 has shown proving result in simultaneous repair/protection of hepatocellular architecture when administered along with contraceptives. Therefore, Liv.52 must be prescribed prophylactically along with the "Dills" which cause predictable injury to the hepatic parenchyma (Khuteta, 1978).

Liv.52 has been shown to be protective in mice against lethal dose of ionizing radiation (Saini et al. 1984). They exposed the male Swiss albino mice to 8.0, 8.5, 9.0 and 10.0 Gy of Co$^{60}$ gamma radiation with and without Liv.52 and reported that control animals showed symptoms of radiation sickness like diarrhoea, anorexia, ruffling of hair and epilation. These were severe as compared to the experimental animals. In some cases the animals had arched backs. It was also found that time of onset and severity of radiation sickness were reduced considerably by the drug.

Radiation sickness and dermatitis were studied by Saini and Kumar (1984) in two groups of adult Swiss albino mice after whole body exposure to three different doses of Co$^{60}$ gamma radiation in the presence and absence of Liv.52 and results from both the groups were compared. It was found that the symptoms of sickness which were noticed in the control animals were not present in the experimental group. In the former the epithelium showed hyperplasia and atypical changes in the cells. The skin appendages were also completely absent. However in the Liv.52 treated animals
the epithelial structure was normal and skin appendages were preserved.

Saini and Saini (1985a) studied the effect of Liv.52 on mammalian liver after whole body exposure to 5.5 Gy of Cobalt-60 gamma radiation. They observed that the drug protected the organ against radiation induced changes. The protective effect was manifested in the form of early recovery as indicated by the absence of pathological change like cytoplasmic degeneration, loss of nuclei from many cells and abnormal architecture at 10 days and restoration of normal structure by 4 weeks.

Pregnant Swiss albino mice were exposed to 2.5 Gy gamma rays with or without Liv.52 during selective organ genesis period by Saini et al. (1985b). They stated that the control pregnant of 11 days gestation showed complete restoration of embryos while drug treated females showed normal parturition. There was no reduction in litter and lateration of sex ratio of newborns. However 25% mortality was recorded within 15 days in the newborns. In most of the remaining animals fusion of the vertebrae was observed in the caudal region.

The radio protective effect of Liv.52 on the peripheral blood of Swiss albino mice was studied on 70 days after exposure to various doses of gamma rays. A significant increase in leucocyte and lymphocyte counts was observed in all the Liv.52 treated animals as compared to the control group. Similarly, the erythrocyte count was also significantly higher in the experimental animals of 9.0 and 10.0
Gy exposed groups in comparison to their corresponding controls. Thus the drug protects the haematopoietic organs against ionizing radiation. The protection is shown by the absence of compensatory reaction in the Liv.52 treated spleen as is evident by their lesser weight and size (Saini et al. 1985c, d).

Jagetia and Ganapathi (1989) evaluated the frequency of micronuclei in bone marrow cells of mice treated or not with Liv.52 and these exposed to 4.5 Gy of gamma radiation from 6 hour to 14 days, post irradiation. The frequency of micronuclei increased from 6 hr to 24 hr post irradiation in both groups and decreased thereafter, the frequency of micronuclei remained significantly lower in the Liv.52 groups. These data demonstrated that Liv.52 protects the bone marrow of mice against radiation injury.

Jagetia and Ganapathi (1991) also studied the induction of chromosomal aberration from ¼ to 14 days of mice treated or not with Liv.52, prior to 4.5 Gy exposure. The frequency of chromatid and chromosomal aberrations started and Liv.52 + irradiated groups. The highest frequency of aberrations was recorded at ½ post exposure which declined after day 1 in both groups. The frequency of both types of aberrations was significantly lower in the Liv.52 + irradiated groups than in the irradiated group.

Jain et al. (1993) evaluated the radiation induced chromosomal aberration in the bone marrow of young adult male Swiss albino mice at 0.5 to 28 days post irradiation. For the study, one group of animals was exposed to 3.6 Gy gamma radiation while other group
received Liv.52 powder orally in 5% dextrose solution for 7 days before irradiation to serve as the experimental groups. The highest frequency of aberrant cells was recorded on day 0.5 on both the groups after which it declined gradually. The number of such cells was significantly less in the experimental group as compared to the control up to day 14 of autopsy, normal values were restored on day 28 in both the groups. Similarly, the incidence of chromatid breaks were highest at days 0.5 and a significant difference between the control and experimental was obtained until day-1 after the exposure followed by a decline to the normal level at day-14 post exposure. The aberration frequency was significantly reduced in Liv.52 treated group in both 0.5 or 1-day autopsy interval. They concluded that Liv.52 excreted its protective effect at the reparative stage of chromosome and pre-treatment with Liv.52 could significantly prevent chromosome from their early radiation damage.

Saini et al. (1994) evaluated the role of Liv.52 treatment in Swiss albino mice during pre and post natal development. Liv.52 drops were given orally to experimental pregnant mice at a dose of 0.25 ml. 1 day/animal through 0-17 of gestation while control animals received an equal volume of tap water in a similar manner. There was a significant increase in the weight of 18 days old foetuses treated with Liv.52 in vitro as compared to the control group. An improvement in the weight was also observed in latter born in Liv.52 administered mice during pregnancy. Resorbed and dead embryos, external malformation in foetuses/offspring and skeletal anomalies in foetuses were absent in these groups.
Moreover, foetuses were absent in these groups. Moreover, foetuses born to Liv.52 treated mothers showed better ossification in the skull bones than the control group. The significant alteration in litter size and sex ratio of the foetuses were noticed in any of these groups. There was no significant variation in weights of the various organs of six weeks old animals born to mother of either group.

Pandey et al. (1994) studied the effect of oral feeding of Liv.52 on lipid peroxidation in normal and damaged liver induced by CCl₄ in albino rats. A small decrease in the level of liver peroxide malondialdehyde (MDA) content in normal liver was observed in Liv.52 fed group which was not dose dependent but MDA levels were significantly decreased when Liv.52 was given to those rats who were having CCl₄ induced liver injury. This response was dose dependent and statistically significant.

Yadav et al. (1994) studied the protective effect of Liv.52 against anti cancer chemotherapy in rats. Histological changes in the liver tissue of the rats were studied after intra peritoneal administration of cyclophosphamide with or without Liv.52 administration when compared with the control group, cyclophosphamide. produced severe fatty changes, diffuse hepatocellular destruction, sinusoidal dilation and congestion in rats. Hepatic changes were reversed remarkably in the Liv.52 treated group and the total leucocyte count (TLC) became near normal. In conclusion, Liv.52 was observed to exert a definite hepatoprotective effect against cyclophosphamide induced hepatotoxicity. The study
demonstrated that Liv.52 drops can be supplemented with anti cancer chemotherapies to decrease the side effects of drugs.

Daga et al. (1995) have used Liv.52 as a dectoxicating agent for haematological constitutes in methyl mercuric chloride (MMC) intoxicated mice. They observed a decrease in various blood parameters (erythrocytes count, Hb and PCV) till day 7 after MMC treatment, following by a recovery but without restoring to normal values even on day 28. On the contrary, ESR level was elevated till day 7, and thereafter declined but failed to reach normal level even till last autopsy interval. When Liv.52 was given prior to MMC treatment, decrease in haematological constituents was significantly less and normal level gained on day 28 by inducing an early recovery. It was concluded that Liv.52 can be used prophylactically against MMC intoxication.

Daga et al. (1995) exposed male Swiss albino mice to 1.20 and 3.60 Gy of whole body gamma irradiation in the presence (experimental) and absence (control) of Liv.52. Quantitative variations in the number of total leucocytes count (TLC) lymphocytes and neutrophils were scored in peripheral blood at various autopsy intervals between 0.5 hours to 28 days. At 1.20 Gy dose, depression in TLC was noticed till day-1, whereas in higher dose until day-5 with a sharpness in 1st 24 hrs. prior administration of Liv.52 significantly prevented the reduction in leucocytes count and initiated recovery. Lymphocytes also declined sharply in both radiation doses upto day-1 and after that showed a recovery towards normal count on day-28 in experimental animals at lower dose. The
behaviour of neutrophils was reciprocal to that of lymphocytes as they showed a rise till day-1 followed by gradual decline up to day-5 leading to a second peak on day-14 in control as well as experimental groups with both the irradiation. Liv.52 helped in restoring normal values of such cells in 1.20 Gy at last autopsy intervals.

Purohit et al. (2001) observed modification of radiation induced biochemical changes in skin of Swiss albino mice by Liv.52. The animals were exposed to three fractions of 1 or 2 Gy of gamma rays at the intervals of 48 hrs. with and without Liv.52. The values of total proteins, glycogen and total lipids increased up to day 3 thereafter, the values declined. Similarly, the values of RNA increased up to day 7, thereafter it declined. Almost normal values were obtained on day 28, whereas, the DNA content decreased up to day 7. After that values increased and reached to the normal level on day 28 in lower dose group. However, the changes were less marked in experimental animals indicated protection by Liv.52.

Purohit et al. (2002) also observed role of Liv. 52 against radiation induced hepatic lesions in Swiss albino mice. They exposed the mice with three fractions of 1 or 2 Gy of gamma rays at the intervals of 48 hrs. with (experimental) and without (control) Liv. 52. The histopathological changes induced distortion of hepatic architecture, intracellular oedema, cytoplasmic degranulation, vacuolation and pycnotic nuclei. The Liv. 52 treated animals showed less severe radiolesions and fast recovery in comparison to control animals.
Purohit et al. (2002) observed protection by Liv. 52 against radiation induced dermatological changes in Swiss albino mice. The animals were exposed to three fraction of 1 or 2 Gy of gamma rays at the intervals of 48 hrs. with and without Liv. 52. The pathology included focal collection of chronic inflammatory cells, shorter dermal papillae and rete pegs, damaged sebaceous glands, hair follicles and thin epidermis. The skin of experimental animals showed less severe radiolesions and early and fast recovery in comparison to control animals.

Vyas et al. (2004) studied modification of radiation and cadmium induced biochemical changes in the brain of Swiss albino mice by Liv.52. They exposed the mice with 5.0 Gy of gamma radiation with or without cadmium chloride treatment. The value of total proteins and cholesterol decreased up to day-7, therefore, the value increased, whereas, the value of glycogen, acid phosphatase and alkaline phosphatase increased up to day-7 then declined in all groups. The severe changes were observed after combined exposure showing synergistic effect. However, the changes were less marked in drug treated animals including protection by Liv. 52.