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Original Article

The Radioprotective Effect of *Aloe vera* in Liver of Swiss albino Mice

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ABSTRACT

The radioprotective effect of *Aloe* leaf extract (1000mg/kg b.wt) was studied in liver of Swiss albino mice before radiation exposure (3 Gy gamma-radiation). Mice were autopsied at day 5 post irradiation and liver was taken for histopathological studies. In this study, appearances of some normal hepatocytes were noticed in both control and experimental sets. Experimental set (*Aloe* extract +irradiation) showed a pronounced recovery in the form of normal cord like appearance of hepatocytes and some other signs. The result of present study suggests that *Aloe vera* has a radioprotective effect due to their antioxidant and radical scavenging activity.

Key Words: Radiation, *Aloe vera*, Histopathological, Radioprotective, Mice

INTRODUCTION

Industrialization and technological areas have amazingly increased the risk of radiation for workers either by chronic and acute exposure. The hazardous effects of radiation on biological systems may be the result of direct and indirect exposure. Degree of direct effect depends on the numbers of a particular type of molecule in the cell and its size. Both direct and indirect effects contribute to overall number of such damaging events to the biomolecules and will vary for individual cell types. When individuals are exposed, the radiation energy is absorbed by the biological systems, which causes radiolysis of tissue water and generates free radicals. The major free radicals such as $O_2^{\cdot}$, $OH^{\cdot}$, $H^{\cdot}$, $HO_2^{\cdot}$, H_3O+ combine with each other and dissolved oxygen to give a variety of potent oxidizing agents such as hydrogen peroxide, molecular oxygen and perhydroxy radicals [1,2,3]. The radiation damage to a cell is potentiated or mitigated depending on several factors, such as the presence of oxygen, sulfhydral compounds and other molecules in the cellular milieu [4,1,2]. The degree and kind of damage vary with dose dependent with dose rate and the types of radiation and also depends on other factors such as age, sex, species and soft tissue of the animals. Effects of high doses are easily seen and can be quantified, because of high incidence of death at these levels. Great vulnerability of the liver to injury by chemical agents emerge to be a consequence of the anatomical position of this organ and the central role it plays in the metabolism and disposition of foreign chemicals [5]. Recent studies have recognized that hepatotoxicity may be inflicting by thousands of synthetic chemicals, environmental pollutants such as radiation and naturally occurring toxicants. Most of the authors consider that liver of young animals is more susceptible to radiation damage. Thus, mammalian liver being a radiosensitive organ may lead to any kind of hepatic injury, which can cause life threatening complications when entire or most of the liver is exposed to ionizing radiation. In most instances, radiation hepatitis occurs in human within 90 days after irradiation [6,7]. Previous studies of Koletsky and Gustafson (1952), Kelly and Hirsh (1955) and Agarwal and Mehrotra (1964) suggested that liver is relatively resistant to radiation injury, while later in clinical as well as animal studies liver was reported to be a very radiosensitive organ [11,12,13,14,15,16].

Besides, the mode of exposure, protection should be provided against harmful effect of ionizing radiation and the integrity of vital tissues must be maintained. For this purpose, discovery of new agents that perhaps would not provide large reduction factor but would be relatively non toxic and useful in specific situations are needed.

Aloe barbedensis (Mill.) belongs to family Liliaceae and commonly known as *Aloe vera*. *Aloe* has been used medicinally for several thousands of

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years. Polysaccharides from *Aloe* are always considered effective radioprotectors on radiation induced skin damage [17]. *Aloe* may be useful in the treatment of acute radiation dermatitis [18]. *Aloe vera* has been claimed to have anti-inflammatory effects and despite a lack of evidence of its therapeutic efficacy, is widely used by patients with inflammatory bowel disease [19].

However, there are limited data regarding the effects of the antioxidant (*Aloe vera*) on physiology of liver system in Swiss mice. Therefore, the objective of the present study was, to test the hypothesis that different dose levels of antioxidant (*Aloe vera)* might effectively protect against radiation or they might induce their side effects.

MATERIALS AND METHODS

Animals: Swiss albino mice of 6-7 weeks old, weighing 24-26 gm were selected for this experimental study. Animals were housed in polyvinyl chloride cages (290 × 320 × 390 mm) and maintained under standard laboratory conditions. The animals had free access to food (mice feed) and water. Tetracycline was also given along with drinking water to them once fortnight as a preventive measure against infection. The maintenance and handling of the animals were done according to the guidelines of the Committee for the Purpose of Control and Supervision of Experimental Animals, Ministry of Environment and Forests, Government of India. All the experimental work was approved by the institutional animal ethics committee.

Source of Irradiation: Animals were irradiated at Cancer Treatment Center, S.M.S. Medical College and Hospital, Jaipur by using Cobalt teletherapy unit (ATC-C9). Animals were kept properly in a well-ventilated wooden box and distance between the animals in wooden box and radiation source was 77.5 cm for exposure at the dose rate of 1.33 Gy / min. The dose rate was calibrated time to time throughout the experimentation according to the decay table of Co^{60}.

Aloe vera: *Aloe barbadensis* (Mill.) belongs to family Liliaceae and commonly known as *Aloe vera.* Plant was collected from surrounding area, identified by the botanist, Department of Botany, University of Rajasthan, Jaipur, allotted identification/voucher number RUBL-19886 and same plant was placed in the departmental herbarium.

Experimental Design: For this study, selected adult male Swiss albino mice were divided into three groups (I, II and III).

Group I: Animals of this group were given double distilled water (DDW) orally (volume equal to that used for *Aloe* administration in experimental mice) for 15 consecutive days and called sham irradiated (normal) group.

Group II: Animals of this group were administered *Aloe* extract orally at the dose of 1000 mg /kg body weight (once in a day) for 15 consecutive days to study its toxic effects on liver.

Group III: Group III was divided into two sets, one was experimental and another was control. Animals of experimental set were administered *Aloe* extract orally at the dose of 1000 mg /kg body weight (once in a day) for 15 consecutive days, whereas animals of control set were given double distilled water (DDW) orally (volume equal to that used for *Aloe* administration in experimental sets) for 15 consecutive days.

Just after 1 hour of last administration of extract and DDW, animals of group III, was exposed to sublethal dose 3 Gy gamma radiation.

Histopathology: A minimum of 5 animals from group II and each set of control and experiment of group III were sacrificed by cervical dislocation on 5^{th} day of post irradiation and liver was taken for histopathological observations.

RESULTS

Radiation sickness is characterized by a definite set of manifestations (signs) of harmful act ion of ionizing radiation such as decrease in food and water intake, diarrhoea, excessive lacrimation, lethargic condition, epilation, ruffling of hair, facial oedema, weight loss etc. Manifestations of signs depend on several factors like whole body or local irradiation single or repeated, acute or chronic exposure and size of exposure dose. In the present investigation, animals from group I (sham-irradiated) showed normal hepatic architecture of liver. No changes were seen in the cytoplasm and nuclei of the hepatocytes. No alterations were observed in the histopathological structure of liver in animals of group II in supplementation of *Aloe* alone for 15 consecutive days. The present study indicates that appearance of some normal hepatocytes, a sign of recovery was noticed in liver of 3 Gy exposed mice at day 5 post irradiation. But normal hepatic architecture was not regained. Degranulation and vacuolization of cytoplasm, fatty degeneration, lymphocytic infiltration, shrunken and crenated nuclei and large number of enucleated hepatocytes were still persisted.

The present investigation in group III showed that, liver of *Aloe* treated 3 Gy irradiated mice showed pronounced recovery at day 5 post irradiation, which manifested in the form of normal cord like appearance of hepatocytes and their normal structure but lymphocytic infiltration, increased binucleated hepatocytes and kupffer cell population was still noticed.

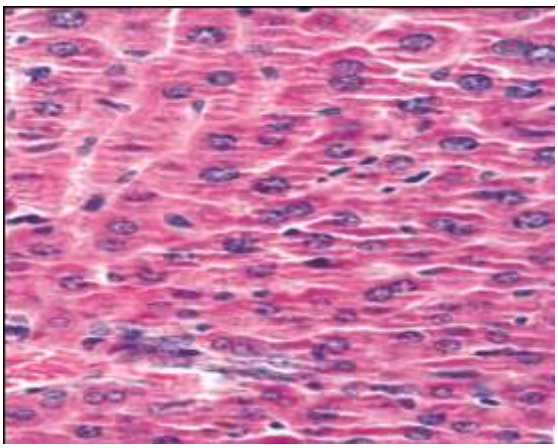

Fig.1. Drug alone

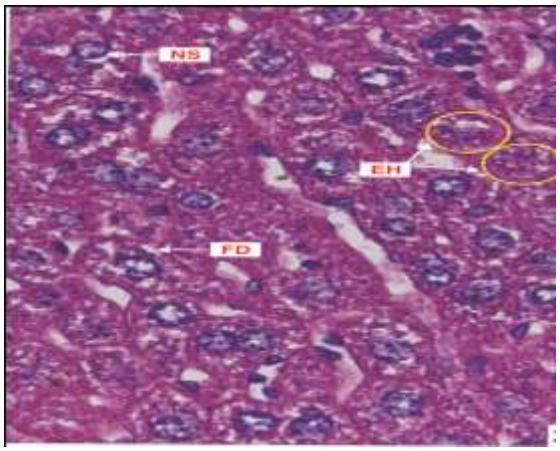

Fig.2. Control Set

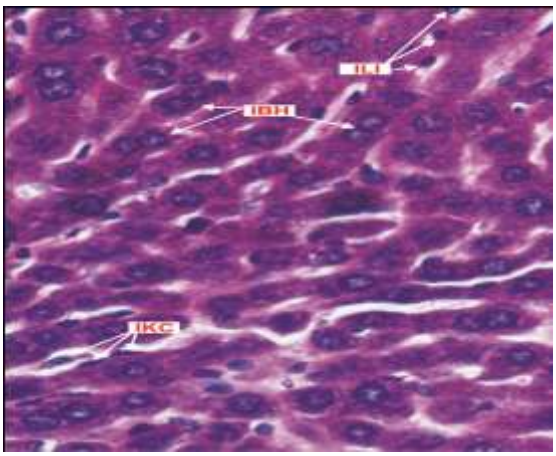

Fig.3. Experimental Set

DISCUSSION

Radiation can cause a variety of symptoms and signs which vary depending on the individual and the duration of exposure. Effects of radiation on liver were not clear in the beginning and therefore it remained a controversial organ for a long time for its radiosensitivity. The mammalian liver has also been reported to be sensitive to internal irradiation. Gupta (1969) observed histological changes in the liver of gerbils injected with very low doses of p32 (0.1 and 0.2 μCi/g b. wt.) [20]. Gupta (1972) and Bhatia *et al.* (1978) reported that mammalian liver is a sensitive organ to internal irradiation at different post-natal ages (1 to 6 weeks) [21, 22]. Therefore in the present investigation, toxic effects of radiation were evaluated; results showed that no changes were seen in cytoplasm and nuclei of the hepatocytes in control group on postnatal day (PND) 5^{th}in liver. Our present findings supported the results of Singh (1979) where we did not observed signs of radiation sickness in those animals exposed to low doses (0.5 and 3 Gy) of gamma radiation [23]. In present study, signs of radiation sickness such as decrease in food and water intake, diarrhoea, weight loss, facial oedema, excessive lacrimation, lethargic condition, epilation, ruffling of hair and weight loss were not observed in those animals exposed to low doses of gamma radiaton (0.5 and 3

Gy) whereas, 5.5 Gy irradiated alone animals showed some signs of radiation sickness like slight decrease in food and water intake, statically insignificant reduction in body weight and mild diarrhoea from day 4 post irradiation and first two signs persisted upto day 10 while, diarrhoea was noticed between day 3-7 post irradiation. 30 days mortality was not observed in animals irradiated with the highest dose of radiation (5.5 Gy). However, Saharan (1977), Saini (1977), Gupta (1980), Maharwal (2002), Jagetia and Baliga (2003) have reported various severe signs of radiation sickness and 30 days mortality because of whole body irradiation of mice with high doses of gamma radiation. Results of this study indicated that exposure of mice to 0.5 and 3 Gy did not because severe damage in both bone marrow and gastrointestinal tract and therefore, signs of radiation sickness did not appear [24,25,26,27].

In the present study, types of histopathological changes and recovery pattern were observed. Although, some signs of recovery such as regranulation of cytoplasm and reappearance of some normal nuclei were noticed at day 5 in liver of 3 Gy exposed mice but hepatic architecture did not regain normalcy; shrunken and crenated nuclei, large number of enucleated hepatocytes and a giant hepatocyte still persisted (Fig.2). However, reappearance of cord like hepatic architecture and presence of normal hepatocytes at day 20 indicated complete recovery in the organ (Fig.3). Similarly, Bhartiya (1970), also reported maximum histopathological changes such as hyperaemia, oedema, lymphocytic infiltration, pycnosis, cytoplasmic degranulation and vaculation at day 2 post irradiation in liver of gerbils exposed to 3 Gy gamma radiation and but resumption of almost normal hepatic picture was reported after one week [11].

Present findings also support to the observation of Grad and Stevens (1950) and Gupta (1969) who also reported severe cytoplasmic degranulation and vacuolation, pyknosis, karyorrhexis, karyolysis, shrinkage and crenation of nuclei in liver cells after internal exposure to p32 [28, 20]. The histological changes observed by all these workers after internal irradiation are basically similar to those observed in the present study after external gamma radiation.
In this study, kupffer cells were seen at day 5 in 3 Gy irradiated animals, in maximum number at day 5 as compare to low dose irradiation on same day to animals at early stage of postnatal life. These findings revealed that increase in kupffer cell population is related to the period of recovery. In this study, *Aloe* extract was tested for providing protection to mice liver against radiation induced injury. The present study showed that supplementation of *Aloe* alone for 15 consecutive days did not change the histopathological structure of liver in Swiss mice. The eminent workers failed to observe any visible pathological change in hepatic tissue following exposure to moderate or large doses of radiations [29]. Studies of Koletsky and Gustafson (1952), Kelly and Hirsch (1955), Agarwal and Mehrotra (1964, 1966) and Gupta (1980) have also shown that liver is relatively resistant organ against radiation [30,31,32,13].

Liver of *Aloe* treated 3 Gy irradiated mice showed recovery process started from day 5 mice but it was more pronounced in *Aloe* treated 3 Gy irradiated mice as compared to high irradiated mice, which was evidenced by the reappearance of normal cord like arrangement of hepatocytes, normal cytoplasmic and nuclear structure but kupffer cell population was still higher, which again showed its relation with recovery process. Similarly, considerably decreased number of enucleated hepatocytes, reappearance of normal sinusoids, hepatic architecture and granulated cytoplasm were the major signs of recovery, noticed at day 5 in *Aloe* treated 3 Gy irradiated mice liver.

Reports of Friedburg (1956) and Doul *et al*. (1961) also showed that herbicide, 3 amino1, 2-triazole provides slight protection to mouse liver against radiation induced damage. Similarly, treatment with cystamine (Chatterjee and Bose, 1962), cysteamine (Eldjarn, 1964) and serotonin (Vittorio *et al*. 1963) provided protection to liver against radiation induced damage, which is in agreement with present findings [33, 34, 35, 36 37].

CONCLUSION

Treatment of mice with Aloe extract for 15 consecutive days did not exhibit toxic effects in liver. Pretreatment of mice with *Aloe* reduced the severity of radiation induced various histopathological changes in liver. Pretreatment also enhanced the recovery process, inhibited increase in kupffer cell population and prevented the formation of radiation induced edematous giant hepatocytes.

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