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Immunomodulatory potential of acemannan (polysaccharide from *Aloe vera*) against radiation induced mortality in Swiss albino mice

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Plant polysaccharides have been reported to stimulate growth, differentiation and proliferation of hematopoietic progenitor and stem cells to protect against the deleterious effects of radiations. This study evaluated the radioprotective potential of acemannan, a major polysaccharide component of aloe vera gel. Treatment of mice with 50 mg/kg body weight of acemannan by oral gavage for 7 days was able to protect against the radiation-induced mortality. Seven-day pretreatment or post-treatment of mice with acemannan resulted in the increase in median survival by 60 and 20%, respectively. The decrease in mortality can be attributed to the induction of hematopoiesis (peripheral lymphocytes counts, spleen cellularity, spleen index) and the upregulation of cytokines like TNF-α and IL-1 by acemannan in irradiated mice. Data indicate that acemannan has the ability to protect mice against radiation-induced mortality by immunomodulation and can be developed as a radiation damage mitigation agent.

Keywords: Aloe vera; polysaccharides; radioprotection; radiotherapy; acemannan

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Introduction

Hematopoiesis and immune depression are well-documented phenomena following radiation exposure. The development of treatment to combat these effects is a challenge for radiation protection as well as radiotherapy of cancers. Damage to proliferating cells results in immune suppression due to depletion of peripheral blood lymphocytes and bone marrow cells, leaving organisms susceptible to various opportunistic pathogens and even some common infection that could become lethal (Goel, Prakash, Ali, & Bala, 2007). Therefore, survival of the animals following irradiation depends on the presence of critical number of the hematopoietic stem cells and their ability to proliferate following stimulation by secreted cytokines. Exogenous treatment with cytokines is reported to have radioprotective effects by inducing the proliferation and recovery of hematopoietic cells resulting in decreased mortality after radiation exposure (Neta, 1988). The recovery of the radiation depleted cells has been reported to take place via autocrine or paracrine mode of action in immune competent mouse (Shukla & Gupta, 2012). However, high toxicity associated with these cytokines has restrained the medical fraternity, to use them in practice (Goel et al., 2007). Therefore,

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development of non-toxic immunostimulatory agents is important for the mitigation of radiation injuries.

In previous studies, polysaccharides extracted from various biological sources such as soybean, *Ocimum sanctum*, ginseng, mulberry leaves, wolfberry, mushroom and fungi have been reported to protect against the radiation-induced damage by regeneration of the hematopoietic stem cells and thus strengthening the immune system and preventing against the immune depression induced by radiation (Kim et al., 2009; Liu, Guo, Zhang, Qin, & Han, 2012; Yao et al., 2011). However, so far discovery of an ideal radioprotector/mitigator has remained elusive.

Acemannan (polyacetylated mannan) is an active component of the gel part of aloe vera leaf and is known to have varied pharmacological properties (Jittapiromsak, Sahawat, Banlunara, Sangvanich, & Thunyakitpisal, 2010; Kahlon et al., 1991; Lee et al., 2001; Peng et al., 1991). It has been reported to have chemotherapeutic properties in mice, canine and feline sarcoma (Harris et al., 1991; Peng et al., 1991). An interesting aspect of acemannan is that, the anticancer activity is not due to cytotoxicity to the cancer cells; instead it is mediated via immunomodulation. It has been shown to promote the infiltration of the immune cells at the cancer site by inducing the secretion of various cytokines resulting in decreased mortality (Harris et al., 1991). Acemannan has been reported to increase the immune response against alloantigen and virus infections also (Womble & Helderman, 1988). Studies *in vitro* have shown that acemannan induced the maturation of dendritic cells, resulting in the amelioration of inflammation in the body by clearing the foreign materials (Lee et al., 2001).

In a preliminary study, done by Roberts and Travis (1995), acemannan reduced radiation-induced skin injury after exposing the skin to 30–47.5 Gy by immunomodulation in C3H mice. Another evidence of radioprotective efficacy came from the study of Egger et al. (1996) showing induction of hematopoiesis in the myelosuppressed mice. Muscatello in a review of nutritional supplements as radioprotectors has mentioned acemannan as a strong possible radioprotective agent for long-term space flight (Muscatello, 1999). However, till date no systematic study has been done to evaluate the role of acemannan as a radioprotective agent.

Therefore, the present study was initiated to evaluate the effects of acemannan on radiation-induced mortality caused by sub-lethal doses of radiation in mice and to understand the mechanisms associated at the cellular and molecular level.

Materials and methods

Extraction of acemannan

Acemannan was extracted from fresh leaves of aloe vera (*Aloe barbadensis*) as described by Ni, Turner, Yates, and Tizard (2004). Stepwise extraction procedure of acemannan from aloe gel is depicted in Figure 1. In brief, full-size mature aloe vera leaves were harvested and the rind was pealed out along with yellow extrude. The remaining portion of gel was soaked in running tap water for 10 minutes and then further kept in the distilled water for another 30 minutes at 4°C to remove the residual portion of the yellow extrude. Colorless parenchyma was scooped out and homogenized at 4°C followed by centrifugation.

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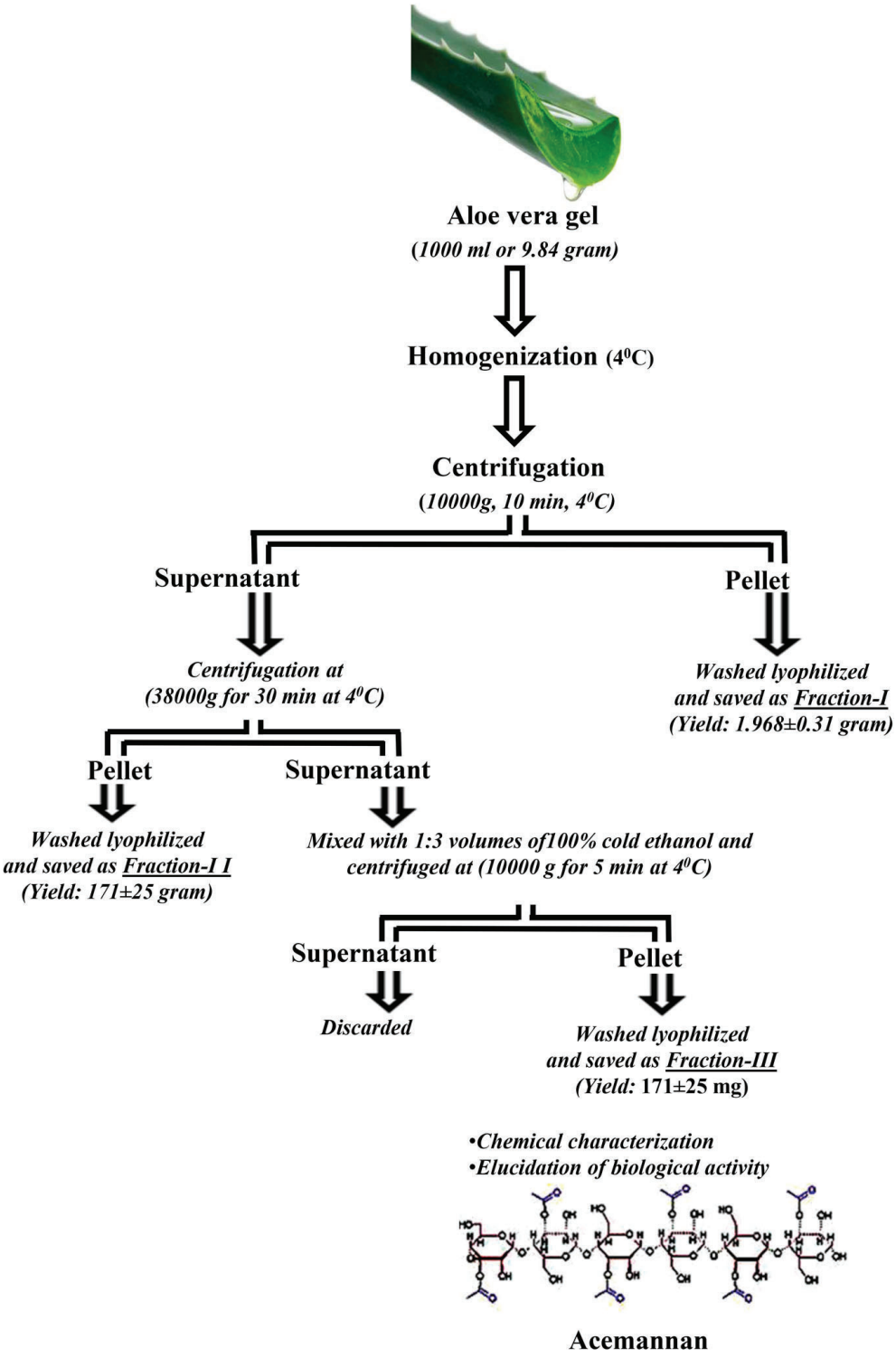

Figure 1. Steps for extraction of acemannan from aloe vera gel.

Determination of total phenolic, flavonoid, carbohydrate and lignin content

The total phenolic content of the extract was calculated as described by Samatha, Acharya, Srinivas, and Ramaswamy (2012) and was expressed as the gallic acid

equivalent (GAE mg/g of test sample). Total flavonoid content (TFC) was estimated as described by Samatha et al. (2012). Absorbance was recorded at 510 nm in a spectrophotometer and TFC was expressed as Quercetin equivalent (Q mg/g of test sample).

Total carbohydrate content (TCC) was determined by anthrone assay as described by Ni et al. (2004). The percentage of carbohydrate present in the sample was calculated using mannose as standard. Lignin was measured as described by Abdel-Halim (2014) with some modifications and lignin content was determined by using the following formula:

$$\text{Lignin content}(\%) = \frac{\text{Weight of precipitate}}{\text{Weight of starting material}} \times 100$$

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Animals

Random-bred male Swiss albino mice (6–8 weeks old) maintained at the university animal house (at 20 ± 2°C, 65–70% humidity and 12 h/12 h day/night cycle) provided with standard food pellets as recommended by the National Institute of Nutrition, Hyderabad, India and tap water ad libitum were used for the study. All the experiments were conducted strictly adhering to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals, constituted by the Animal Welfare Division, Government of India and Institutional Animal Ethics Committee (IAEC) on the use of animals in scientific research. The experimental protocols were approved by the IAEC-JNU (Jawaharlal Nehru University).

Experimental design

For the present study, the mice were divided into the following groups: Group I: Sham control (given water orally); Group II: Radiation control (5 Gy exposure); Group III: Drug control [7 days oral treatment of acemannan (50 mg/kg)]; Group IV: Drug + Radiation [7 days acemannan treatment (50 mg/kg) prior to radiation exposure of 5 Gy]. Mice were placed inside the ventilated perspex containers and exposed to whole body radiation in a gamma chamber using cobalt-60 (Bhabhatron 4000A, Department of Atomic Energy, India) at a dose rate of 2.14 Gy/min. Following irradiation, animals were kept in animal house and sacrificed by cervical dislocation at different time points for examination of different parameters.

Isolation of splenocytes and cell proliferation assay

Spleens were removed after 3 hours of irradiation from mice and splenocytes prepared and cultured as per Sharma and Tiku (2014). Cell proliferation was evaluated using MTT assay originally described by Mosmann in 1983. In brief, 20,000 spleen cells were seeded in 96-well ELISA plate and incubated for 24/48 hours. Twenty microliters of MTT (Sigma-Aldrich, USA) solution (5 mg/ml in culture medium) was added to the wells 4 hours prior to the end of incubation. The culture medium was removed by spinning the ELISA plate at 1870 g for 5 min at 4°C. Acidified DMSO (1% of 1 N HCl in DMSO) was added to each well and absorbance was measured at 560 nm.

Endogenous spleen colony assay

Spleen colony and spleen index were calculated as described by Kunwar et al. (2010). In brief, animals were sacrificed at the 11th day post-irradiation. The spleen was dissected out, washed in saline, blotted and weighed. The spleen index was calculated as follows

$$\text{Spleen Index} = \frac{\text{Weight of spleen}}{\text{Total body weight}} \times 100$$

The spleens were then fixed in the Bouin's fixative (Saturated picric acid 30.0 ml + Formaldehyde 10.0 ml + Glacial acetic acid 2.0 ml) for 15 min and colonies counted with the help of hand-held magnifying glass.

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Peripheral blood cell counting

Blood was collected from the tail vein of the mouse and transferred into EDTA-coated vials. For lymphocyte counting, 10 µl of blood was mixed with 190 µl of RBC lysis buffer (388 mM NH_4Cl, 29.7 mM $NaHCO_3$, 25 µM Na_2EDTA). After incubation for 1 minute, cells were counted using hemocytometer.

Assessment of serum cytokines

To measure the cytokines in serum of animals, mice were anesthetized by using isoflurane. The blood was collected from heart by syringe and transferred in the heparin-coated tubes. The serum was collected from blood after a brief centrifugation (22000g for 5 minutes at 4°C). The cytokines (IL-1, IL-6 and TNF-α) were measured by commercially supplied kit as per the manufacturer's instructions [558075 Mouse IL-6 In Vivo Capture Assay Set, 559603 OptEIA™ interleukin-1β, 555268Mouse TNF (Mono/Mono) ELISA Set from BD bioscience, USA].

Animal survival

To study the effectiveness against the radiation-induced mortality, *in-vivo* survival studies were carried out as described by Kulkarni et al. (2013). The effect of acemannan on radiation-induced mortality was studied in pre- and post-irradiation treatments. Mice were divided into 10 groups (10 mice each) as follows:

Sham control: mice were given saline orally

Radiation control: mice were exposed to radiation (6, 9 or 12 Gy) and monitored daily for 30 days.

Pre-irradiation treatment: mice were given acemannan (50 mg/kg) for 7 days by oral gavages and irradiated (6, 9 or 12 Gy).

Post-irradiation treatment: mice exposed to radiation (6, 9 or 12 Gy) and immediately after radiation were given acemannan (50 mg/kg) for 7 days by oral gavage.

To calculate LD50/30 (lethal dose expected to kill half of the population in 30 days), percentage of surviving mice was plotted in the linear plot and the dose that killed 50% mice was calculated for radiation control and drug + radiation groups. The level of significance was calculated using log-rank (Mantel–Cox) test and p-values <0.05 were considered as significant. The dose reduction factor (DRF) was

calculated as the ratio of the LD50/30 of radiation + acemannan-treated mice to the LD50/30 of radiation + saline-treated mice.

Statistical analysis

Mean and standard deviation was calculated using Graph pad prism 5.03. Statistical analysis was done using normality test followed by Mann–Whitney rank sum test. The values are mean ± SD and p-values <0.05 were considered as significant.

Results

Chemical analysis of the fractionated portion of the aloe vera gel

The three fractions collected from the aloe vera gel were further analyzed for carbohydrate, flavonoids, phenol and lignin content (Table 1). Fraction III contained the highest carbohydrate and total phenolic content among all fractions. Other two fractions contained relatively low carbohydrate content (9–12%) and were thus rejected. Fraction III with about 50% carbohydrate content was used for further studies and will be called as acemannan here after.

Effect of acemannan on cell proliferation in splenocytes of irradiated mice

Splenocytes isolated from mice exposed to radiation (5 Gy) showed a reduction in the cell proliferation by 8.5 and 12.1% after 24 hours and 48 hours, respectively, in comparison to unirradiated control (Figure 2(a)). The mice pretreated with acemannan prior to irradiation showed an increase in proliferation by about 5.7 and 7.1% after 24 and 48 hours in comparison to irradiation control, respectively. However, this change in proliferation was not significantly different from the control groups.

Effect of acemannan on endogenous colony formation

Radiation exposure resulted in the reduction of body as well as spleen weight. The spleen index was reduced after 30 days of irradiation. However, mice treated with acemannan for 7 days before irradiation had higher splenic index and overall improved health status (Figure 2(b)). Acemannan alone did not have any effect on splenic index. The number of colonies formed in spleen following irradiation indirectly

Table 1. Chemical analysis of the fractionated portion of the aloe vera gel.

	Chemical constituents (%)			
Fractions from Aloe Gel	Carbohydrate*	Flavonoid^	Phenolics$	Lignin (%)
Fraction I	11.3% ± 0.68	0.6% ± 0.003	3% ± 0.031	0.03
Fraction II	9.88% ± 0.38	0.055% ± 0.001	2.4% ± 0.017	0.01
Fraction III	51.4% ± 0.2.53	0.13% ± 0.007	3.89% ± 0.26	0.001

Note: Each value represents mean ± SD of experimental data performed in triplicates.
^Equivalent to Quercetin standard.
$Equivalent to Gallic acid standard.
*Equivalent to Mannose standard.

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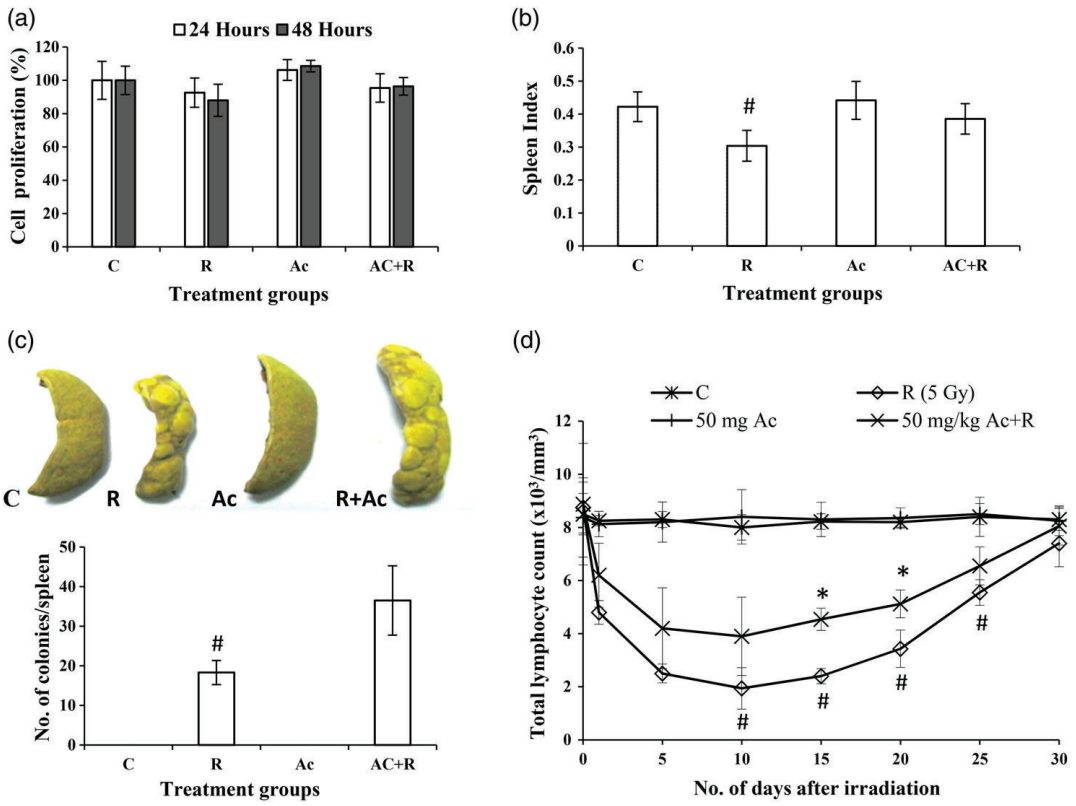

Figure 2. Effect of acemannan pretreatment for 7 days on hematopoietic parameters of whole body irradiated mice. (a) Proliferation of spleen cells after 24 and 48 hours, (b) spleen index (11th day post-irradiation), (c) micrographs and bar diagram showing endogenous colonies in spleen (11th day post-irradiation, 6 Gy), (d) lymphocyte count for 30 days post-irradiation. C, sham control; R, radiation control (5 Gy); Ac, acemannan (50 mg/kg) only; Ac + R, acemannan + radiation. Each data point represents mean ± SD ($n = 10$). #Significant at $p < 0.001$ compared to unirradiated control; *Significant at $p < 0.05$ in comparison to irradiated control.

gives an assessment of the surviving cells in the hematopoietic system. Spleen colonies were observed in mice exposed to radiation (6 Gy) and an average of 18 ± 3 colonies were observed per mouse (Figure 2(c)). The number of colonies was significantly increased to almost double (36 ± 8/mouse) in mice treated with acemannan for 7 days prior to irradiation.

In addition, changes in lymphocyte count were also monitored over a period of time. At Day 1 post-irradiation, the leukocytes count decreased by 41% and further decreased by 70% at Day 10 in comparison to unirradiated control. However, after the 10th day, the leukocytes count started increasing and reached up to 89% at the 30th day (Figure 2(d)). In mice that were given acemannan for 7 days prior to radiation exposure, leukocyte count was 29% higher than the radiation control. The gap between the leukocyte recovery in radiation control and acemannan with radiation group started widening up to the 10th day. However, after that the difference started decreasing and reached up to 8% at Day 30 post-irradiation, showing that recovery was faster in acemannan-treated group. No significant difference was observed in the level of leukocytes between the untreated control and only acemannan-treated mice during the above period.

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Effect of acemannan on cytokine secretion

Cytokines are pleiotropic in nature and regulate many essential processes in the body such as hematopoiesis and immune response. Radiation induces the expression of pro-inflammatory cytokines (TNF-α and IL-6). In the present study, we observed a 2.34 and 1.32-fold increase ($p < 0.05$) in the level of TNF-α and IL-6, respectively, in comparison to unirradiated controls at the 7th day of irradiation in mice serum (5 Gy) (Figure 3(a) and 3(b)). The level of IL-1 was found to reduce by 40 ± 4% in comparison to control at the 7th day following radiation exposure. Acemannan treatment to the mice prior to irradiation further enhanced the level of TNF-α, but IL-6 was found to reduce. Similarly, the level of IL-1 was also found to increase significantly in comparison to the irradiation control (Figure 3(c)). Acemannan alone at (50 mg/kg) enhanced the level of IL-1 and TNF-α significantly ($p < 0.05$) in unirradiated mice. No significant change in the level of the IL-6 was observed in unirradiated mice treated with acemannan.

Since an increase in the level of TNF-α and IL-1, an inflammatory cytokine, was induced by acemannan, we studied the effect of acemannan on the level of nitric oxide (NO), another marker of inflammation in biological systems. An increase of 28% ± 2 was observed in the level of NO in the hepatic tissue after 24 hours of radiation

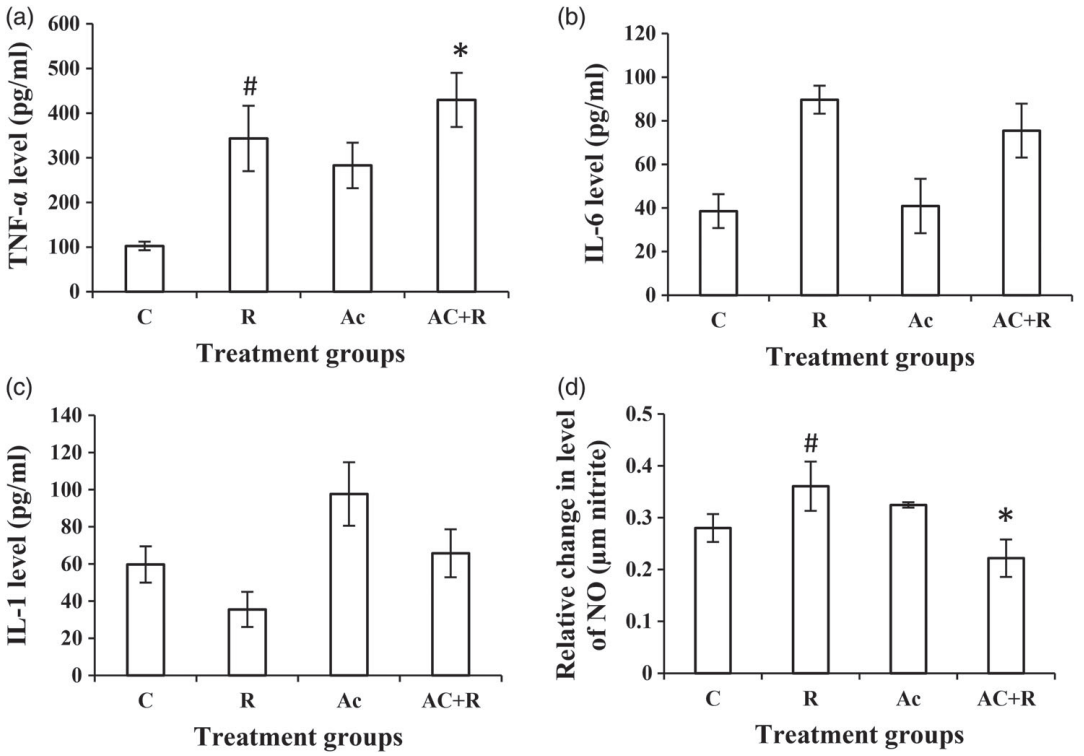

Figure 3. Modulation of Pro and anti-inflammatory cytokine levels, measured in serum of WBI mice pretreated with acemannan. (a) TNF-α, (b) IL-6, (c) IL-1 (The levels were measured in blood on the 7th day post-irradiation), (d) effect of acemannan on radiation-induced nitric oxide level in mice hepatic tissues. C, sham control; R, radiation control (5 Gy); Ac, acemannan (50 mg/kg) only; Ac + R, acemannan pretreatment. Results are presented as mean ± SD ($n = 6$). #Significant at $p < 0.001$ compared to unirradiated control; *Significant at $p < 0.05$ in comparison to irradiated control.

exposure (Figure 3(d)). The level of radiation-induced NO was found to reduce by 33.4% in mice that received acemannan treatment before irradiation.

Effect of acemannan on radiation-induced mortality

The mice were exposed to different doses of radiation (6, 9 and 12 Gy) and survival was monitored for 30 days. Mortality increased with increasing dose of radiation. Only 60% mice could survive till Day 30 in the group of mice exposed to 6 Gy, while the group exposed to 9 Gy showed only 30% survival. None of the mice could survive till Day 30 in the 12 Gy group. The rapid mortality was seen between the 4th and the 12th day in all groups and continued up to Day 19 at lower doses. On the contrary, treatment with acemannan before irradiation with 6, 9 and 12 Gy resulted in the reduction of mortality from 40 to 10%, 70 to 30% and 100 to 60%, respectively (Figure 4(a)). The LD50/30 increased from 7 to 11 Gy in the acemannan-pretreated group. The DRF was found to be around 1.57 (Figure 4(c)).

In post-irradiation treatment studies also, survival of the mice increased in all the three treatment groups. In the present study, acemannan administration reduced the

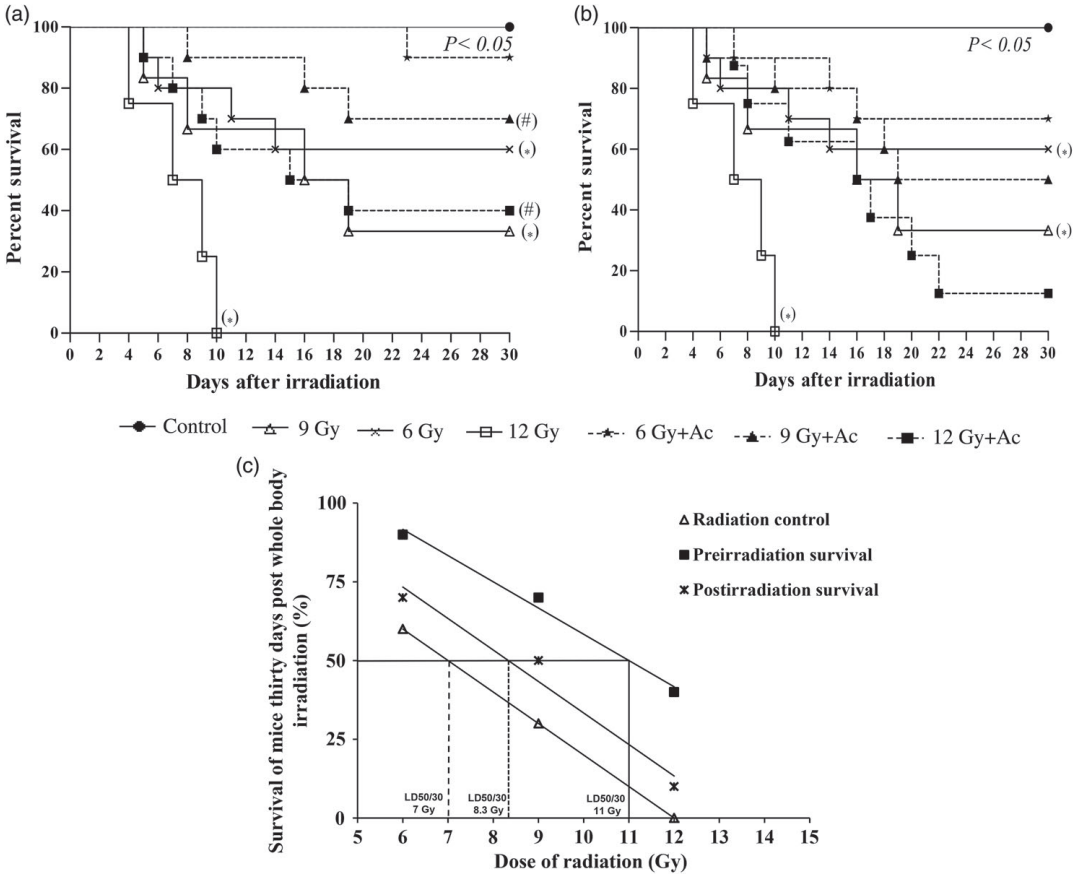

Figure 4. Effect of acemannan (50 mg/kg) on the survival of whole body-irradiated mice at different doses of radiation (6, 9, 12 Gy). (a) Pretreatment for 7 days, (b) post-treatment for 7 days, (c) DRF (Dose Reduction Factor) estimated as the ratio of the $LD_{50/30}$ value of radiation in the drug-treated group to the untreated group. ($n = 10$). *Significant in comparison to unirradiated control, #Significant in comparison to irradiated control.

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mortality from 40 to 30%, 70 to 50% and 100 to 90% at 6, 9 and 12 Gy, respectively, in 30 days after irradiation (Figure 4(b)). The LD50/30 increased to 8.3 Gy in the acemannan post-treated group from 7 Gy in radiation control. The dose-reduction factor was found to be around 1.2 (Figure 4(c)).

No death was observed after Day 19 in acemannan post-irradiated mice; however, the mouse death occurred till Day 22 in the post-treatment group.

Discussion

In the present study, we evaluated the effect of different doses of the polysaccharide component acemannan extracted from the aloe vera gel on the radiation-induced damage in mice. Chemical analysis of fraction III (acemannan) used for the present study consisted of carbohydrates and had only negligible amount of the other biological impurities such as phenols, flavonoid and lignins. The major sugar present in acemannan is reported to be mannose (62.9%), along with few other sugars in minor proportions such as glucose (13.1%) and galactose (0.6%) (Ni et al., 2004). This β-(1, 4) acetylated mannose has been reported to help in the regeneration of the damaged tissues by inducing the proliferation of hematopoietic cells (Jittapiromsak et al., 2010). Therefore, the presence of acetylated mannose in the extract used in the present study could lead to observed increase in the survival of mice. Damage to lymphoid organs by radiation is the main cause of death of the exposed organism and modulation of hematopoietic system could have an important role in radioprotection (Karkanitsa, 1997).

In the present study, acemannan pre- as well as post-treatment was found to induce radioprotection. Our results showed a higher levels of circulating lymphocytes in the acemannan-pretreated mice in comparison to mice exposed to only radiation. The proportion of circulating lymphocyte count started decreasing from Day 1 to Day 10 post-irradiation in both acemannan + radiation and radiation-alone groups. However, the proportion of decrease in lymphocytes was much less in the acemannan-pretreated mice. After Day 10, the lymphocyte count started increasing in both the groups and reached almost equal to the control on Day 30 post-irradiation, but the rate of recovery was higher in the acemannan-pretreated mice. This faster recovery of the depleted lymphocyte could be due to the protection against radiation-induced hematopoietic injury or due to induction of hematopoiesis.

To further confirm, we checked the endogenous spleen colony formation and spleen index since both are important parameters to study the recovery from hematopoietic injury (Kunwar et al., 2012). The spleen index of acemannan-pretreated mice showed an increase in comparison to radiation-alone treated group. This increase was concomitant with the increase in endogenous spleen colony formation suggesting that acemannan stimulates the growth of hematopoietic stem cells. In previous studies, acemannan has been shown to induce the proliferation of dental pulp cell and bone marrow stromal cells (Boonyagul, Banlunara, Sangvanich, & Thunyakitpisal, 2014; Jittapiromsak et al., 2010). The radioprotective effect of various aloe vera components has been reported and attributed to many biological activities, like scavenging of free radicals, inhibition of apoptosis, protection against radiation-caused bacteremia and antiprostaglandin effects (Bruce, 1967; Pande, Kumar, & Kumar, 1998; Saini & Saini, 2011; Wang et al., 2004). However, the exact mechanism of action has not been elucidated so far. The acetylated mannose which mimics the bacterial O-linked mannose to activate

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hematopoietic cells can result in the immunostimulatory activity of acemannan (Lee et al., 2001; Reynolds & Dweck, 1999).

Cytokines and growth factors are important mediators of host defense and their role in modulating radiation response is well known (Singh & Yadav, 2005). Neta et al. (1991) reported that treatment of mice with IL-1 antibodies reduced the survival of irradiated mice by 50% and thus endogenously produced cytokines can contribute to the resistance from damaging effects of radiation. IL-1 is produced by monocytes and macrophages and stimulates the bone marrow to overcome the radiation-induced myelosuppression (Constine et al., 1991). Besides stimulating the proliferation of cells, IL-1 can also induce the quiescent early progenitor cells to enter into the cell cycle, possibly into the S phase, radioresistant phase (Neta 1997a). In the present study, acemannan-treatment enhanced the level of the radiodiminished IL-1 which perhaps resulted in the increased survival of mice.

TNF-α is also known to act as a facilitator and inhibitor of the hematopoiesis and is strongly induced by radiation (Rübe et al., 2002; Slordal, Warren, & Moore, 1990). Following irradiation, induction of the inflammatory response induces hematopoiesis or production of new cells resulting in increased survival (Slordal, Muench, Warren, & Moore, 1989). However, with increasing dose of the radiation, inflammation itself starts acting as a causative agent of mortality (Zhang, Xing, & Lawrence, 2007). In both processes, TNF-α acts as the main agent. Besides, TNF-α, which is secreted by mononuclear phagocytes, also acts on stem cells, through secondary hematopoietic cytokines, produced by bone marrow stromal cells (Neta, 1997b).

We observed a synergistic induction of TNF-α and IL-1 by acemannan resulting in the improved survival of mice in comparison to radiation alone group. IL-6 is another pleiotropic cytokines which is known to cause inflammation. In the present study, acemannan reduced the expression of the IL-6 following irradiation indicating its protective effects. Acemannan has also been reported to induce the release of the cytokines such as IL-6, IFN-γ and TNF-α from the RAW 264.7 (macrophage) *in vitro* (Zhang & Tizard, 1996). Furthermore, acemannan may modulate the immune system by binding with the lectin receptors as already reported for many polysaccharides having similar structure (Tzianabos, 2000).

Immunomodulators are also known to cause inflammation which may have additive effects on compromising the quality of life of the exposed individuals following induction of radiation-induced nitric oxide (Luster, 1998; Ong et al., 2010). The radiation-induced NO is known to produce RNS after interacting with ROS, such as superoxide ($O2^{-}$) (Rabender, Alam, & Mikkelsen, 2014). Although radiation-induced NO is shown to activate different stress proteins, including MAPK and JNK, which have cyto-protective effects, its ability to increase the blood flow and RNS production suppresses its usefulness (Rabender et al., 2014). Acemannan reduced the level of radiation-induced NO in the WBI mice in comparison to radiation control group suggesting that acemannan-induced cytokines do not contribute to the induction of inflammation, but on the contrary promote the hematopoiesis. The reduction in the NO could be due to chelation of Fe++ by acemannan (data not shown), which is required as a co-factor for iNOs gene transcription (Goel et al., 2007). Chen et al. (2005) have also reported that the aloe polysaccharides do not contribute to nitric oxide production.

Acemannan decreased the mortality considerably in treated groups in comparison to the radiation-alone control groups. The calculated DRF was found to be 1.56 in the

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pretreatment and 1.18 in the post-treatment groups. Present study further indicates that death resulted in the initial 4th to 10th day due to hematological damage, because the reduction in the number of lymphocytes continued up to Day 10. Hematopoiesis was further confirmed by the post-irradiation studies where acemannan could increase the survival of mice. Although the pattern of mortality was similar in both the post- and pretreatment groups, however, the onset of symptoms of morbidity were delayed in the acemannan-pretreated group in comparison to the post-treated group. Treatment with acemannan resulted in the reduction of the LD50/30 dose of radiation from 7 to 11 Gy and 8.3 Gy in pre- and post-irradiation treatment groups, respectively. Saini and Saini (2011) have also shown that the 15-day pretreatment of mice with dry aloe vera gel powder at 750 mg/kg body weight resulted in the increase in LD50/30 dose from 6.77 to 10 Gy. Low toxicity of acemannan even at oral dose of 2000 mg/kg/day for 6 months as reported by Williams et al. (2010) further increases its superiority over the synthetic radioprotectors/immunomodulators.

In conclusion, we have demonstrated that acemannan derived from widely used aloe vera gel exerted its radioprotective effects in the pre- and post-irradiation treatment in mice. The acemannan treatment resulted in the increase in the survival by protecting against radiation damage by upregulating the immune system and inducing proliferation of the hematopoietic cells in WBI mice. Further, acemannan has been shown to protect the animals in the post-irradiation studies and is non-toxic at high doses, hence can be exploited as a radiation mitigating agent in case of unplanned exposures.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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