International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Ionizing Radiation in Space: Protecting Human Biochemistry During Long-Duration Missions

Aahana Mittal

Email: *aahanausgs[at]gmail.com*

Abstract: ***Space exploration exposes astronauts to ionizing radiation from galactic cosmic rays, solar particle events, and trapped radiation belts, posing significant risks to human biochemistry. This review examines the molecular and cellular impacts of space radiation, including direct DNA damage (e. g., single- and double-strand breaks), indirect oxidative stress via reactive oxygen species, and protein alterations, which increase risks of cancer, neurodegeneration, and cardiovascular dysfunction. Drawing on the NASA Twins Study, the paper highlights real-world evidence of radiation-induced changes in gene expression, telomere dynamics, and inflammation during long-duration spaceflight. Current and emerging protective measures are evaluated, including physical shielding (e. g., hydrogen-rich materials), operational strategies (e. g., mission timing), and pharmacological interventions (e. g., Amifostine, melatonin, MnSOD mimetics). The review synthesizes findings from peer-reviewed studies to underscore the need for a multifaceted approach to mitigate radiation effects for future lunar and Martian missions. By integrating insights from radiobiology and materials science, this work emphasizes the critical role of interdisciplinary strategies in safeguarding astronaut health. The findings are relevant to medical science and space exploration, offering a foundation for developing effective countermeasures to ensure the safety of humans in deep space.***

Keywords: Space radiation, DNA damage, oxidative stress, astronaut health, protective measures.

1. Introduction

Space is a uniquely hostile environment for human biology, and one of its most significant threats comes in the form of cosmic radiation. Unlike on Earth, where the atmosphere and magnetic field provide substantial protection, astronauts are exposed to a constant stream of ionizing radiation from galactic cosmic rays (GCRs), solar particle events (SPEs), and trapped radiation belts (Durante & Cucinotta, 2008). This radiation comprises high-energy particles; including protons, alpha particles, and heavier ions such as iron, that interact with biological tissues at the molecular level, triggering a series of complex biochemical changes (Cucinotta & Durante, 2006).

Ionizing radiation affects human biochemistry both directly and indirectly. Direct interactions occur when radiation deposits energy directly into critical biomolecules like DNA, causing strand breaks and base alterations (Sridharan et al., 2015). Indirect effects stem from the radiolysis of water, generating reactive oxygen and nitrogen species (ROS and RNS) that propagate widespread damage throughout cells (Azzam et al., 2012). These biochemical disruptions can result in mutations, impaired cellular signalling, apoptosis, and altered metabolic processes (Wang et al., 2021).

The impact of cosmic radiation is influenced by several variables, including the type and energy of the radiation (reflected in its linear energy transfer, or LET), duration of exposure, and individual susceptibility. High-LET particles such as HZE ions are particularly destructive due to their dense energy deposition along short paths (Yatagai et al., 2019). These interactions can trigger persistent oxidative stress, protein misfolding, membrane damage, and inflammation; factors linked to accelerated aging, cancer risk, cardiovascular dysfunction, and neurodegeneration (Cucinotta et al., 2011).

This section introduces the overarching biological threats posed by space radiation, providing a foundation for the detailed examination that follows. Specifically, this paper seeks to understand how cosmic radiation alters human biochemistry at the molecular and cellular levels, and what strategies can be employed to mitigate these effects during long-duration spaceflight. This focus is critical as future missions aim to take astronauts farther from Earth's protective atmosphere for extended periods, increasing their exposure to hazardous radiation. Subsequent sections will explore the mechanisms of radiation-induced cellular damage, case studies of astronaut physiology, and current and emerging protective measures, including pharmacological interventions, spacecraft shielding, and lifestyle strategies.

Impact on Human Biochemistry:
Space radiation comprises a complex mixture of high-energy particles, including protons, helium ions, and heavier atomic nuclei known as HZE ions. These particles possess energies capable of penetrating spacecraft shielding and interacting with biological tissues, initiating a cascade of biochemical reactions at the cellular level that can have both immediate and long-term consequences for astronaut health. This includes DNA Damage, Oxidative stress, and Protein Alterations (NASA, n. d.).

Direct DNA Damage:
Direct effects arise from the direct ionization or excitation of atoms and molecules within the cell by the traversing radiation particle. This is particularly significant for critical biomolecules such as DNA, where the direct deposition of energy can lead to structural alterations, including strand breaks and base damage (Swarts et al., 2007).

Linear energy transfer is an important factor to consider. High LET radiation, like HZE ions, deposits substantial energy over short distances, resulting in dense ionization tracks that are more damaging to biological tissues. In contrast, low LET radiation, such as gamma rays, causes more isolated damage that cells can often repair more effectively (Cucinotta & Durante, 2006).

Indirect Effects:
Indirect effects are initiated by the interaction of ionizing radiation with water molecules, which constitute the majority of cellular content. This process, known as radiolysis, leads to the formation of highly reactive oxygen species (ROS) such as hydroxyl radicals (•OH), superoxide anions ($O_2^{\bullet-}$), and hydrogen peroxide (H_2O_2), as well as reactive nitrogen species (RNS). These free radicals are highly unstable and can readily react with a wide range of cellular components, including DNA, proteins, and lipids, causing significant damage. In fact, indirect effects mediated by ROS are estimated to account for approximately 60–70% of total radiation-induced cellular damage (Spitz et al., 2004). The prevalence of water within cells makes this indirect pathway a major contributor to the overall damage from space radiation.

Single Strand Breaks (SSBs): SSBs involve the breakage of one strand of the DNA double helix and can result from direct ionization or ROS interaction. Efficient repair mechanisms exist, but accumulation of SSBs can lead to genomic instability (Caldecott, 2008).

Double Strand Breaks (DSBs): Double-Strand Breaks (DSBs): Double-strand breaks are considered the most detrimental type of DNA lesion, characterized by the breakage of both strands of the DNA molecule. They can lead to mutations, chromosomal translocations, or cell death if not properly repaired (Pommier et al., 2016).

Base Modifications: Space radiation can also induce various types of base damage in DNA, including oxidation, alkylation, and deamination. These modifications can result from direct ionization of the DNA bases or indirectly through the action of ROS.

Oxidative Stress
Oxidative stress, characterized by an imbalance between the production of reactive oxygen species (ROS) and the ability of the cellular antioxidant defense system to neutralize them, is a significant consequence of exposure to space radiation.

The elevated levels of ROS resulting from space radiation exposure can trigger a cascade of damaging reactions within human cells. These highly reactive molecules can directly damage DNA, leading to single and double-strand breaks, as well as base modifications. Furthermore, ROS can induce protein oxidation, leading to modifications like carbonylation and nitration, which can alter protein structure and function.

Chronic oxidative stress is associated with inflammation, aging, and increased risk of cancer and neurodegenerative diseases (Zhang et al., 2025; Valko et al., 2007). Notably, space radiation has been shown to elevate specific biochemical markers of oxidative stress and inflammation, such as interleukin-6 (IL-6), 8-hydroxy-2′-deoxyguanosine (8-OHdG), and malondialdehyde (MDA), all of which are associated with DNA damage, lipid peroxidation, and cellular aging (Zwart et al., 2013; Cui et al., 2011).

Astronaut Case Studies
The NASA Twins Study, involving twin astronauts Scott and Mark Kelly, is a landmark investigation that provides insights into the effects of long-duration spaceflight on the human body (NASA, 2019). Analyzing the study is a key step toward understanding the effects of radiation on human biochemistry. Identical twins like Scott and Mark Kelly share nearly the same genetic makeup, providing a unique opportunity to minimize the influence of genetic variability in research. This allowed NASA to isolate the effects of spaceflight by comparing Scott's experiences in space with Mark's on Earth (Garrett, 2018).

Scott Kelly spent 340 consecutive days on the International Space Station (ISS) from March 2015 to March 2016, while Mark Kelly remained on Earth as the control subject (NASA, 2019).

Key Findings
Significant changes in gene expression were observed in Scott during his time in space. Approximately 91.3% of these changes returned to baseline after his return to Earth; however, a small subset of genes remained altered, indicating potential long-term effects (Garrett-Bakelman et al., 2019). Notably, many of the affected genes were involved in pathways related to DNA repair, immune function, inflammation, and oxidative stress response, suggesting that spaceflight-and specifically, radiation exposure, can exert lasting effects on critical cellular systems.

Scott's telomeres (protective caps at the ends of chromosomes) lengthened during his time in space, which was an unexpected finding. Upon his return to Earth, his telomeres quickly shortened, in some cases becoming even shorter than their pre-flight lengths. While telomere dynamics can be influenced by both radiation and physiological stress, the transient nature of these changes and their correlation with oxidative stress suggest that radiation may have played a role (Garrett, 2018; Garrett-Bakelman et al., 2019).

Scott's cognitive performance remained largely stable in space. However, a decline in speed and accuracy was observed after his return to Earth, though this eventually normalized (NASA, 2019). Significant changes were also observed in Scott's gut microbiome, likely due to the controlled diet on the ISS. These changes reversed upon his return to Earth (Garrett-Bakelman et al., 2019).

Scott experienced other physiological changes as well, including fluid shifts, decreases in bone density and muscle mass, and vision alterations, all of which are consistent with the effects of microgravity. Additional effects included increased inflammation and thickening of the carotid artery walls, both of which are also potentially linked to radiation-induced oxidative stress and vascular remodeling (Garrett-Bakelman et al., 2019).

Protective measures and strategies against space radiation
Physical Shielding

Traditional Materials:
While commonly used in spacecraft construction, aluminum, a traditional material, is not very effective against high-energy space radiation, particularly galactic cosmic rays (GCRs) (Pinsky et al., 2020; NASA, 2024). Hydrogen-rich materials like water are more effective at absorbing radiation. Water can

serve dual purposes as shielding and a vital resource. (Durante & Cucinotta, 2008; NASA, 2024). Polyethene is also rich in hydrogen and offers better shielding properties than aluminum. (Durante & Cucinotta, 2008)

Advanced Materials:
Ongoing research is exploring polymers with enhanced hydrogen content for better GCR attenuation while maintaining structural flexibility (Pinsky et al., 2020). Combining multiple materials (e. g., polyethylene with boron-rich layers) can optimize shielding while reducing spacecraft mass (Yamashita et al., 2022).

Shielding Placement:
Shielding is strategically placed around sensitive areas such as crew quarters and electronics. Consumables like water can also be positioned to act as temporary shielding (NASA, 2024).

Operational Strategies
Missions are planned to avoid solar maximum phases, when solar particle events (SPEs) are most frequent (NASA HRR, 2024). Moreover, shorter missions can significantly reduce total radiation exposure (NASA HRR, 2024). Trajectories can be optimized and mission paths are designed to limit time spent in high-radiation zones like the Van Allen belts (NASA HRR, 2024).

Biological Countermeasures: Protective Drugs (Summarised in Table 1)

Radioprotectors: These drugs aim to prevent or reduce radiation damage if administered *before* exposure.
Radiomitigators: These drugs are given *after* exposure to lessen the severity of radiation-induced injuries.

Promising Drugs and Mechanisms:

Amifostine:
An FDA-approved drug for protecting against radiation damage during cancer therapy. Amifostine is a prodrug that is metabolized to an active thiol metabolite, WR-1065. This metabolite neutralises free radicals; unstable and highly reactive molecules, promotes DNA repair, and can also modulate cellular signaling pathways involved in radiation response. Amifostine has its side effects such as nausea and hypotension which pose as challenges for space use (NCI, 2024).

Melatonin:
A naturally occurring hormone with antioxidant properties, melatonin reduces oxidative stress and inflammation and has shown efficacy in radiation mitigation (Reiter et al., 2014). Melatonin can reduce oxidative stress caused by radiation, protect DNA, and modulate immune function. In animal studies, melatonin has demonstrated protective effects against radiation-induced damage. For instance, in a study by Vijayalaxmi et al. (1998), melatonin administration in mice prior to whole-body irradiation reduced DNA damage by approximately 60% as measured by micronuclei frequency in bone marrow cells. Melatonin has relatively low toxicity, is non-carcinogenic, and is already clinically used to treat sleep disturbances, making it a promising candidate for space applications.

Manganese Superoxide Dismutase (MnSOD) mimetics:
These synthetic compounds mimic the activity of MnSOD, a key antioxidant enzyme located in mitochondria. By targeting mitochondria, where a significant portion of radiation-induced reactive oxygen species (ROS) is produced, these mimetics offer a potentially more effective approach to reducing oxidative stress. Research suggests that MnSOD mimetics can protect against radiation-induced cardiovascular damage, neurodegeneration, and carcinogenesis. In summary, they mimic mitochondrial manganese superoxide dismutase, targeting reactive oxygen species (ROS) and offering tissue-specific protection against radiation-induced cardiovascular and neurological damage (Greenberger et al., 2021). They may offer more targeted and effective antioxidant protection compared to some other antioxidants.

Polyphenols:
Natural antioxidants like resveratrol and curcumin exhibit anti-inflammatory properties and may enhance DNA repair, offering a promising avenue for dietary radioprotection (Di Pietro et al., 2021)

Other Potential Agents:
These include Cytokines in which growth factors such as erythropoietin (EPO) and G-CSF can boost blood cell production, mitigating hematopoietic damage from radiation (Seetharam et al., 2008). DNA repair enhancers are also a viable option. Drugs that augment DNA repair enzyme function can help cells recover from ionizing radiation exposure (Epperly et al., 1988).

Table 1: Comparison of Promising Radioprotective and Radiomitigative Agents

Drug/Agent	Mechanism of action	Pros	Cons	Stage of Testing / Use
Amifostine	Prodrug, WR-1065. Scavenges free radicals; promotes DNA repair	FDA-approved; effective radioprotection in cancer patients	Side effects: nausea, vomiting, hypotension	Clinical use in cancer therapy; experimental for space
Melatonin	Antioxidant; reduces ROS; modulates immune and DNA repair pathways	Low toxicity; non-carcinogenic; 60% DNA damage reduction in irradiated mice	Short half-life; limited large-scale human data	Preclinical/animal studies; widely used for sleep
MnSOD Mimetics	Mimic mitochondrial antioxidant enzyme; target ROS at source	Tissue-specific protection (heart, brain); may reduce cancer risk	Experimental; limited human data	Preclinical studies (Greenberger et al., 2021)
Polyphenols (e. g., resveratrol, curcumin)	Antioxidant & anti-inflammatory; potential to modulate DNA repair enzymes	Natural, dietary; multiple health benefits	Low bioavailability; needs formulation enhancement	Preclinical and nutraceutical research

Cytokines (e. g., EPO, G-CSF)	Stimulate blood cell production, mitigate hematopoietic injury	Clinically used in other contexts; protect bone marrow	Can promote tumor growth; costly	Clinical for other diseases; experimental for space
DNA Repair Enhancers	Boost activity of repair enzymes (e. g., ligases, endonucleases)	Target root cause of damage; potential synergy with antioxidants	Experimental; specificity and delivery challenges	Experimental/preclinical

Lifestyle and Nutritional Changes

An Antioxidant-Rich Diet; diets high in vitamins C and E, selenium, and carotenoids may protect cells from radiation-induced oxidative stress (Widel, 2020). Moreover, specific nutrients such as Omega-3 fatty acids are being studied for their neuroprotective and anti-inflammatory roles in radiation defence (Khan et al., 2019).

Risks of Some Drugs

Amifostine (WR-1065), while effective, the side effect profile is a major concern for long-duration space missions. Research is focused on developing analogues or delivery systems that minimize these side effects. Studies have shown that Amifostine can protect against a range of radiation-induced damage, including hematopoietic (bone marrow), gastrointestinal, and pulmonary injuries.

2. Conclusion

As humanity explores space farther, understanding and mitigating the effects of cosmic radiation on human biochemistry becomes not just a scientific necessity, but a survival imperative. As discussed, ionizing radiation in space disrupts cellular processes through direct DNA damage and indirect oxidative stress, increasing the risk of long-term health consequences such as cancer, neurodegeneration, cardiovascular disease, and premature aging. Astronaut case studies; especially the NASA Twins Study, highlight the profound biochemical and physiological changes triggered by prolonged spaceflight, even in highly trained and healthy individuals.

Although space agencies have made significant strides in developing protective measures, challenges remain. Current shielding materials and mission planning strategies offer partial protection but are insufficient against the high-energy particles of galactic cosmic rays. Therefore, a multifaceted approach; combining advanced physical shielding, operational tactics, pharmacological countermeasures, and targeted lifestyle interventions-is essential for sustainable human space exploration.

The future of space travel depends on our ability to bridge the gap between the known risks and the development of reliable counterstrategies. Continued research in radiobiology, biochemistry, and materials science will be crucial in safeguarding astronaut health on missions to the Moon, Mars, and beyond. As we push the boundaries of human presence in space, we must equally advance our understanding of how to preserve life amidst the most extreme conditions in the cosmos. Future studies could also explore novel avenues such as gene-editing techniques to enhance cellular resistance to radiation, or the development of biomaterials that mimic natural antioxidant defenses.

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