Positive Spin: Analysis of Pharmaceutical Degradation due to Heavy Ionising Radiation Exposure and its Impact on Pharmaceutical Stability and Viability in Future Space Exploration and Habitation

Astraea Technologies

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Abstract

As human space exploration advances towards missions to the Moon, Mars, and beyond, the health and safety of astronauts remain paramount. A critical challenge is the impact of space-related heavy ionising radiation on pharmaceuticals intended to maintain crew health during long-duration missions. Astraea Technologies plays a pivotal role in bridging existing knowledge gaps by advancing space medicine research focused on the effects of cosmic radiation on drug stability. This paper discusses the unique radiation environment of space, highlights the challenges associated with pharmaceutical degradation under these conditions, and demonstrates how Astraea Technologies' research and technology development align with international recommendations to ensure the efficacy and safety of pharmaceuticals in space.

Introduction

The safe and healthy travel of astronauts on missions beyond low-Earth orbit (BLEO) requires extensive research into the effects of space radiation on human health and medical countermeasures, particularly pharmaceuticals. Historically, space missions have relied on frequent resupply of medications, minimising concerns about their long-term stability in space. However, upcoming extended missions necessitate a robust understanding of pharmaceutical stability under the harsh radiation conditions unique to space. Astraea Technologies, a pioneer in space technology and research, has recognised this need and is actively contributing to addressing these critical challenges.

Human spaceflight is projected to expand significantly in the coming years (Borowitz et al., 2023). Unlike the majority of previous missions, upcoming crewed launches will venture into BLEO. A notable example is the Artemis program, which aims to establish a permanent lunar base as part of its long-term objectives (Cohen, 2023). This program marks a significant milestone in human space exploration and is intended to serve as a precursor to deeper space expeditions, including missions to Mars. A critical challenge that must be addressed when sending astronauts into BLEO is the mitigation of space radiation exposure.

2. The Space Radiation Environment and Its Challenges

2.1 Overview of Space Radiation

"Daily exposure to cosmic radiation is also a natural part of the environment in which we live. Until recent decades, it was considered to be of minor relevance, as Earth's magnetic field and atmosphere provide protection from cosmic radiation. Now, however, over 500 astronauts have gone beyond this protection and faced significantly higher cosmic radiation dose rates, and this number will increase in the future. This specific circumstance was addressed in Publication 123 entitled 'Assessment of radiation exposure of astronauts in space' (ICRP, 2013)."

Astronauts in space are exposed to a complex mix of radiation, including:

- **Galactic Cosmic Radiation (GCR):** A chronic, isotropic background of high-energy protons (≈85%), helium nuclei (≈14%), and heavier ions.
- **Solar Particle Events (SPEs):** Sporadic, intense bursts of protons, helium, and heavy ions.
- **Secondary Radiation:** Particle fragmentation (spallation) occurs when primary cosmic rays interact with spacecraft materials, generating a cascade of secondary particles.

Unlike terrestrial radiation exposure, which is mitigated through time, distance, and atmospheric shielding, astronauts and materials in space experience doses that can exceed 75-100 mSv on a six-month International Space Station (ISS) mission, and even higher (>2000 mSv) on extended interplanetary journeys. The International Commission on Radiological Protection (ICRP) is the primary body in protection against ionising radiation. The ICRP recommends that humans should only be exposed to ≤50 mSv annually. According to the ICRP Guidelines, human exposure to radiation is categorised by three different situations:

1. Planned exposure situation: In this type of radiation exposure, radiation sources are intentionally introduced and operated. Security screening is an example of planned radiation exposure.
2. Emergency exposure situation: This kind of radiation exposure situation requires urgent action to limit or reduce undesirable consequences.

3. Existing exposure situation: The prolonged radiation exposure after an emergency situation falls under the existing exposure situation category.

The Commission considers exposure to cosmic radiation, including that produced by solar flares, as an existing exposure situation.

Exposed individuals are categorised as follows:

1. Occupational exposure: When individuals are exposed to radiation from work.
2. Medical exposure: Medical exposure mainly concerns patients, caretakers of patients who are not in a medical occupation, or volunteers conducting biomedical research for some other potential beneficiaries.
3. Public exposure: All exposures other than occupational and medical exposures.

Specific to the space environment, in a report published by the ICRP, detailing their recommendations for radiological protection from cosmis radiation in aviation, the Commission recommends that exposure be maintained as low as reasonably achievable with a dose reference level selected to take into account the level of exposure of the most exposed individuals who warrant specific attention in the particular circumstance, typically in the 5–10 mSv year-1 range (Sage, 2016).

The Commission considers exposure to cosmic radiation, including that produced by solar flares, as an existing exposure situation. The Commission continues to consider that the exposure of all aircraft passengers, both occasional and frequent flyers for personal reasons or professional duties, should be regarded as public exposure, and that the exposure of aircraft crew should be treated as occupational exposure.

Given the apparent global commitments outlined by numerous Space agencies and private space companies, both qualified astronauts and space tourists will need to be considered when determining radiation protection measures.

Current planned missions

Mission	Organisation	Human Category

Artemis	NASA	Astronauts
Mars	SpaceX	Astronauts & Space Tourist

It is logical to conclude that if humans are committed to space missions, their protection must also be a priority. Under the Universal Declaration of Human Rights, article 24:

"Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control." (UDHR, 1948).

In alignment with this Declaration, there should be a global effort to ensure the health and well-being of humans who venture beyond LEO so as to ensure they thrive, rather than just survive in space.

Thanks to the introduction of modern medicine, many people can flourish even when they harbour serious medical conditions. The privilege afforded to humans stemming from modern medicine should also extend into human existence off-world. The examination of the space environment on these pharmaceuticals, and the subsequent optimisation of these products for human use in space, should be a fundamental priority for all organisations aiming to continue delivering humans to the space environment.

2.2 Pharmaceutical Stability Concerns

Radiation exposure can impact pharmaceutical stability through:

- **Direct Ionisation:** Breaking chemical bonds in active pharmaceutical ingredients (APIs).
- **Indirect Ionisation:** Generating reactive free radicals (e.g., ROS) that can degrade drug formulations, especially in liquid-based drugs.
- **Spallation Effects:** Enhanced complexity of ion species, particularly in solid formulations, can induce unforeseen degradation.

When a pharmaceutical compound is exposed to heavy ionising radiation, such as protons or alpha particles, the high-energy particles transfer a significant amount of energy to the molecules, disrupting their chemical bonds and causing structural damage. Spectroscopic methods, including Fourier-transform infrared (FTIR) and Raman spectroscopy, provide a powerful tool to observe these radiation-induced changes. By analysing the shifts and changes in the absorption or scattering peaks of a molecule's unique spectral "fingerprint," researchers can identify which specific functional groups or bonds are most susceptible to degradation. This technique offers a non-destructive way to monitor the molecular stability of a drug both in real-time and after exposure, providing a detailed molecular-level view of the radiation's effect.

This type of analysis is not merely an academic exercise; it has critical implications for practical applications, particularly for medicine in extreme environments. For instance, in long-duration space missions, where astronauts are exposed to cosmic radiation, understanding the stability of life-saving medications is paramount to ensuring their efficacy. By pinpointing the weak points in a drug's molecular structure, scientists can work to develop more stable formulations or protective packaging. Furthermore, this research informs the safe handling of radiopharmaceuticals and other drugs used in nuclear medicine. Ultimately, the insights gained from spectroscopic analysis under radiation contribute to a more comprehensive understanding of molecular radiochemistry and enable the design of safer, more resilient therapeutic agents for future use.

Despite studies using terrestrial radiosterilisation doses (25-50 kGy) showing relative stability, these exceed space mission doses (≈0.5 Gy) and may not adequately simulate chronic, low-dose-rate exposures encountered in deep space. This discrepancy highlights the pressing need for dedicated research to simulate the space radiation environment accurately.

There is a paucity of evidence regarding pharmaceutical stability in the space environment, largely because this issue has not historically been a pressing concern for human spaceflight. Short-duration flights of the Mercury, Gemini, Apollo, and Space Shuttle eras minimised the need for prolonged medication shelf life, and the selection of healthy crewmembers minimised the need for ongoing medication provision for chronic disease. Careful maintenance of crew health and stringent flight rules regarding the more dangerous activities during spaceflight, such as extravehicular activity (EVA), have largely obviated the need for emergency medication provision. Even now, with missions to the International Space Station (ISS) lasting 6 months or longer, crews have been able to rely on medication availability through retirement of expired medications and frequent resupply rather than contending with questions of degradation, storage, and the impact of the space environment (with environmental concerns related to a myriad of factors such as vibration, humidity, and space radiation exposure). As a result, investments in the systematic collection of data for the characterisation of medication use, efficacy, side effects, pharmacokinetics, pharmacodynamics, and long-term stability have been a lower priority than other health and human performance investments. With the push for exploration missions to the moon and Mars, these questions have become a more pressing concern.

2.3 Challenges in Emulating the Space Environment

Accurate simulation of the complex space radiation environment for pharmaceutical testing via terrestrial analog is currently not possible, given limitations in radiation type and dose rate of exposure. Unfortunately, there is only limited documentation regarding research design or even the full results of this study, limiting our ability to fully interpret findings from the GCR simulator at the NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory in Brookhaven, New York. To date, the NSRL is the only U.S. government facility capable of generating heavy-charged particles at energies and spectra that approximate the space environment. As NASA looks towards the challenges associated with missions involving increased distance from Earth, the current inability to provide a safe and effective pharmacy for exploration spaceflight has been identified as a major research gap. To address this issue, NASA recently developed a Pharmacy Research Plan in which pharmaceutical stability and radiation risk are highlighted as unknowns that should be addressed in dedicated research efforts prior to lunar or Mars missions. However, this research plan faces challenges, including approaching mission design-freeze deadlines and a need to declare a planned formulary for fast-approaching exploration missions, expected to occur within the next decade of spaceflight.

Despite decades of pharmaceutical use in spaceflight, there is limited knowledge regarding alterations of pharmacokinetics (absorption, metabolism, and excretion of a medication) and pharmacodynamics (drug effects on the body) in the space environment. As the human body undergoes significant physiological and metabolic changes during spaceflight, it stands to reason that the effects of pharmaceuticals on an astronaut may change during flight. However, research on this issue has largely been limited to observational reports and analog studies. Without directed studies to examine the multifactorial impact of the space environment on pharmaceutical response, it is difficult to fully understand how the additional risks from space radiation may further alter drug response, if at all, during exploration missions.

Successful mitigation of radiation risk relies upon a more thorough understanding of the potential effects of radiation upon pharmaceuticals, insight regarding which pharmaceuticals are at highest risk for radiation-induced damage, and an awareness of how the myriad of spaceflight-related factors (e.g. altered pharmacokinetics and pharmacodynamics, radiation dose, radiation dose-rate, packaging, shelf life, etc.) affect an exposed drug. Careful and controlled study of pharmaceutical stability, with ground controls and appropriate sample size, would greatly improve our understanding of the multifactorial risks to pharmaceuticals in space. Additional ground-based studies comparing the effects of gamma, x-ray, or electron beam to proton or heavy ion exposure may improve understanding of how to better translate terrestrial literature to the context of space radiation. Utilisation of the ISS as a research platform, with long-duration storage of pharmaceuticals and well-designed and controlled studies of shelf life and radiation exposure, could provide much-needed understanding of stability in actual spaceflight conditions. However, such studies would need to be initiated rapidly, as the ISS is intended for decommissioning within the next decade. With rapidly approaching exploration mission dates, NASA and its international partners seek a mature pharmaceutical formulary that can be realised before vehicle and mission design freezes occur.

Ultimately, this pharmacological inquiry paves the way towards an examination of the complex physiological interplay of pharmaceuticals when exposed to heavy ionisation radiation. This positions an astronaut-centered approach to missions.

3. Astraea Technologies: Advancing Research and Innovation

3.1 Bridging the Knowledge Gap

Astraea Technologies, in collaboration with the University of South Australia's Centre of Pharmaceutical Innovation, is at the forefront of efforts to understand and mitigate the risks associated with pharmaceutical degradation due to space radiation. Through interdisciplinary collaboration, Astraea Technologies is developing advanced ionising radiation detection technologies to quantify the types and intensities of radiation impacting pharmaceuticals onboard spacecraft. This work is critical for ensuring that astronauts have access to safe and effective medications throughout the duration of their missions. In addition, Astraea Technologies pioneers ground-based studies using simulated space radiation spectra. These studies include chronic low-dose-rate exposures and mixed-field irradiation, which better replicate the complex conditions encountered during actual space missions. Such experiments allow researchers to more accurately predict how pharmaceutical compounds might degrade or lose potency in space. Moreover, Astraea Technologies integrates these terrestrial analog studies with pharmacokinetic and pharmacodynamic evaluations, investigating potential interactions between radiation exposure, drug formulation, and astronaut physiology. By combining laboratory simulation with advanced modelling of human responses, the company aims to ensure that medications remain stable, effective, and safe for use in the demanding environment of space travel.

3.2 HIRO-LAB

Astraea Technologies Heavy Ionising Radiation Observation Laboratory (HIRO-LAB) leverages the degradation effects of heavy ionising radiation in testing chambers and outside of the Earth's magnetosphere on pharmaceuticals to advance stability and reliability for future missions. The miniaturised spectrophotometer accurately analyses the rate of pharmaceutical decay through exposure to heavy ionising radiation, while the radiation sensor gathers key radiation levels throughout the mission. Examining the effects of Galactic Cosmic Rays and Solar Particle Events that are commonly encountered throughout BLEO missions, these modular earth-based and deep space environments allow the gathering of more data on the lifespan and degradation of pharmaceuticals. This will allow for future refinement and testing to provide safer pharmaceuticals for manned missions to the Moon and Mars.

3.3 Contributions to International Best Practices

Astraea Technologies aligns its research initiatives with recommendations from the International Commission on Radiological Protection (ICRP) and national space agencies, ensuring that its work addresses the most pressing needs in astronaut health management and pharmaceutical safety. A key area of focus is the establishment of pharmaceutical safety thresholds for medications used at BLEO. By defining acceptable limits of pharmaceutical degradation and potency loss, the company supports safe and effective medication use on long-duration space missions. Astraea Technologies also prioritises the identification and validation of biomarkers that can serve as early indicators of pharmaceutical degradation. These biomarkers enable rapid, non-invasive monitoring of medication stability, allowing for timely interventions to maintain drug efficacy. Additionally, the company is actively involved in developing radiation risk models that integrate both deterministic and stochastic effects. These models contribute to comprehensive predictive frameworks that guide astronaut health management, ensuring that pharmaceutical safety remains a cornerstone of mission success. Through this multifaceted approach, Astraea Technologies demonstrates its commitment to advancing the safe use of pharmaceuticals in the unique environment of space.

3.4 Synergies with Space Medicine Research

Astraea Technologies' work contributes directly to:

- **Radiation Biodosimetry:** Supporting accurate dose estimations and personalised risk assessments for astronauts, essential for both pharmaceuticals and overall health.
- **Pharmaceutical Formulary Development:** Informing the design of a safe and effective pharmacy for exploration missions by identifying medications most susceptible to radiation-induced degradation.
- **Radiation Protection Strategies:** Contributing to the development of effective shielding materials and packaging solutions that reduce exposure to both astronauts and pharmaceuticals.

4. Conclusion and Future Directions

As humanity's ambitions extend towards the Moon, Mars and beyond, the challenges of pharmaceutical stability under space radiation become increasingly critical. Astraea Technologies' contributions to this field through the development of innovative detection technologies, research aligned with international standards, and predictive models are indispensable to ensuring astronaut health and mission success. Future work will focus on:

- Expanding studies to include more complex space radiation simulations, such as concatenated SPE and GCR exposures.
- Collaborating with international partners to develop comprehensive guidelines and pharmaceutical safety standards for BLEO missions.

By investing in this crucial research, Astraea Technologies is helping to secure the health and success of astronauts - and by extension, advancing both space medicine and human health on Earth.

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