RADIATION IMPACT ON PHARMACEUTICAL STABILITY: RETROSPECTIVE DATA REVEIW

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PURPOSE

Historical studies performed by the JSC Pharmacotherapeutics Discipline suggest that exposure to spaceflight conditions may compromise the safety and efficacy of some medications. Follow-on studies have revealed that affected medications demonstrate reductions in active pharmaceutical ingredient (API) concentrations and altered release characteristics. It was hypothesized that the changes in API potency and release were from the medication's exposure to the harsh environmental conditions of spaceflight. Subsequent review of the spaceflight environmental control records from the time of these studies indicated that temperature and humidity levels aboard all spacecraft remained within United States Pharmacopeia (USP) recommended ranges to maintain optimal pharmaceutical stability. Therefore, space radiation was presumed to be the source of observed drug degradation. The Pharmacotherapeutics Discipline conducted a ground analog radiation experiment in 2006 at the NASA Space Radiation Laboratory (NSRL) at Brookhaven to validate this theory and to characterize the effects of high-energy radioactive particles on pharmaceutical stability. These data were never published. Recently, the Exploration Medical Capability (ExMC) Element finalized a research plan (RP) aimed at providing a safe and effective medication formulary for exploration spaceflight. As ExMC begins to design new flight and ground analog radiation studies, further analysis of the 2006 NSRL study data is essential for the characterization of the impact of radiation on medication potency and efficacy in the exploration spaceflight environment.

METHODS

The study design, raw data, and analytical results of the 2006 NSRL radiation analog study were reviewed. The materials used during this study included: eight medication test kits (6 irradiated, 2 controls) containing 18 medications of various dosage forms and therapeutic classes selected from previous International Space Station (ISS) or Space Shuttle medication formularies (2006); a radiation dosimeter; and a remote temperature and relative humidity logging device (HOBO®, model U12-011). The experimental study design included two arms (experimental irradiation arm, non-irradiated control arm) maintained under identical environmental conditions (location, temperature, humidity). Radiation arm study samples were exposed to 1GeV/amu iron (Fe) and 1 GeV proton (P) radiation at doses of 10cGy, 10Gy, and 50Gy for each beam type. The beams were independently measured using Al2O3:C Optically Stimulated Luminescence Detectors (OSLDs) to confirm dosage. Stability-indicating tests performed on the medications included Liquid Chromatographic (UPLC or HPLC) API content analysis, solid and semi-solid dosage form dissolution (dissolution apparatus/ultraviolet analyzer) and diffusion rate analysis, visual inspection, and tablet hardness and friability analysis, and were based on USP standard analytical methods and product acceptance criteria.

RESULTS

After iron irradiation, five of the 18 medications tested (28%) had a $\geq$ 5% reduction in their respective label-claimed API content. After proton irradiation, seven of the 18 medications tested had a $\geq$5% reduction in their respective label claimed API content. Eight of 11 tablets demonstrated changes in physical appearance, uniformity, or hardness, and six tablets failed USP acceptance criteria for API release. At the time of the NSRL study there were no U.S. Food and Drug Administration (FDA) or USP guidelines available for establishing diffusion criteria for the semi-solid medications. However, three of the 5 semi-solid medications tested had altered release rates from those of their matching controls.

CONCLUSION

Uncertainty regarding space radiation effects on medication degradation and potency remains high, though these data suggest that space radiation may affect the potency and quality of some pharmaceuticals. This uncertainty warrants further empirical measurements to characterize this risk area for long-duration planetary missions. In the absence of obtaining such characterizations from actual spaceflight exposures, high-fidelity space environmental analogs or ground-based targeted radiation exposure could provide useful insights, improving our ability to provide a safe and effective exploration mission medication formulary.

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