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## A QUALITATIVE SYSTEMATIC REVIEW EVALUATING THE IMPACT OF ELEVATED AMBIENT CO2 IN ATMOSPHERE ON PHARMACEUTICAL STABILITY

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**INTRODUCTION:** Pharmaceuticals are an essential component of the medical system for crewed missions. Current research has identified decreased stability in space-flown pharmaceuticals compared to ground controls, and this presents a significant risk for future exploration-class missions where resupply will be limited. While the cause is not known, the elevated ambient carbon dioxide (CO2) in the spacecraft atmosphere has been postulated as a potential contributing factor. The aim of the review was to determine the impact of higher partial pressure of carbon dioxide in the atmosphere on pharmaceutical stability from the available literature.

**METHODS:** An extensive search was conducted on the Ovid MEDLINE, Ovid EMBASE, Cochrane Library (Wiley), Web of Science Core Collections (Clarivate Analytics), PubSpace, and the NASA Technical Reports Server (NTRS) databases from the beginning of records to April 6, 2020. Abstract screening was performed on the results in a blinded manner by two authors (KP, BC) and secondary screening by full text was performed in a blinded manner by another two authors (AY, RV, ES). The Aerospace Medicine Systematic Review Group (AMSRG) quality scoring tool was used to assess the quality of included documents and NVivo 12 was used to extract data for thematic analysis.

**RESULTS:** The systematic review identified a total of four publications of varying quality out of a total of 13,385 documents. There was insufficient data to complete a quantitative comparison. A thematic analysis was conducted and revealed two overarching themes: 1) Elevated levels of ambient CO2 may be a precipitating factor leading to pharmaceutical degradation and 2) that pharmaceutical repackaging may lead to accelerated degradation profiles.

**DISCUSSION:** The lack of quality studies in both terrestrial and space environments affirm a literature gap in understanding the effect of elevated ambient CO2 on pharmaceutical stability. Furthermore, space-flown pharmaceuticals are repackaged for missions due to operational purposes and there is terrestrial literature reporting limited stability for pharmaceuticals that were repackaged on the ground in dosage administration aids. Further studies are needed to elicit the individual impact of higher ambient CO2 and repackaging on pharmaceutical stability.