Abstract: Cardiovascular and numerous metabolic diseases in Navajo nation residents near the Grants Mining District (GMD) are closely related to the uranium-containing respirable dust. Many studies have focused on understanding the fate of the inhaled dust particles in various lung conditions and their subsequent impact on humans. However, our understanding on the chemistry behind the uranium leaching from larger-sized (typically <10 µm) dust particles cleared to the human gastrointestinal tract (GIT) remain scarce. In the current study, we evaluate the uranium solubility of dust collected from five sites near the Jackpile and St. Anthony mines in the GMD using two simulated gastrointestinal fluids in fasted-state conditions: Simulated Gastric Fluid (SGF) and Simulated Intestinal Fluid (SIF). The dissolution of uranium from dust, at least in part, depends on the mineralogy of the dust itself. Further, geochemical calculations performed with PHREEQC 3.3.8 suggest that the dust samples enriched with andersonite, Na₂Ca(UO₂)(CO₃)₃.6H₂O, have higher uranium dissolution in SIF compared to that of SGF. The presence of kaolinite and microcline significantly impact the uranium leaching by each fluid. These geochemical calculations are in good agreement with the experimentally observed results. Finally, this study gives insight into the mineralogy-controlled toxicological assessment of uranium-containing inhaled dust cleared to the gastrointestinal tract.