Public Abstract
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Title:Generation of DNA-Damaging Reactive Oxygen Species via the Autoxidation of Hydrogen Sulfide under Physiologically Relevant Conditions

Hydrogen sulfide is commonly known as a toxic, foul smelling gas. In recent years, it has come to light that this small, gaseous molecule could be a cell-signaling agent. Furthermore, recent evidence has shown that hydrogen sulfide is a DNA-damaging mutagen as well. In this work, the chemical mechanisms of DNA-damage by hydrogen sulfide was examined using a plasmid-based DNA cleavage assay. We found micromolar concentrations of hydrogen sulfide caused single-strand DNA cleavage. Mechanistic studies showed this process involves the autoxidation of hydrogen sulfide to generate several reactive oxygen species, including superoxide, hydrogen peroxide, and finally hydroxyl radical, a well-known DNA-damaging agent. DNA strand cleavage occurred even in the presence of physiological thiol concentrations. It was also demonstrated that the known oxidative by-products of hydrogen sulfide, including thiosulfate, sulfite, and sulfate do not cause strand cleavage. This autoxidation process could help to explain some of the genotoxic and cell-signaling properties of hydrogen sulfide.