Olfactory Toxicity of Inhaled Hydrogen Sulfide

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Hydrogen sulfide (H\textsubscript{2}S) is an important air pollutant produced by a variety of anthropogenic and natural processes associated with the decomposition of organic matter. Ambient air H\textsubscript{2}S concentrations range from 0.1 to 4 parts per billion. This chemical is also produced by anaerobic bacteria in the mouth and gastrointestinal tract. H\textsubscript{2}S is a potent inhibitor of cytochrome oxidase and is associated with dysosmia and anosmia in humans and nasal lesions in exposed rodents. Studies conducted at CIIT have shown that subchronic inhalation exposure of male rats to $\geq 30$ parts per million (ppm) H\textsubscript{2}S [No Observed Adverse Effect Level (NOAEL) = 10 ppm] results in widespread sensory neuron loss and basal cell hyperplasia in the olfactory mucosa. Other CIIT studies have shown that H\textsubscript{2}S-induced olfactory injury primarily occurs along high-flux areas within the nose and may be associated with H\textsubscript{2}S-induced inhibition of cytochrome oxidase and subsequent hypoxemia. The overall goal of this project was to further characterize the dosimetry and nasal toxicity of H\textsubscript{2}S. Recent ACC-funded research has focused on (a) determining whether altered tissue pH occurs in the rat nasal epithelium following H\textsubscript{2}S inhalation; (b) determining whether gene expression changes in the rat nasal epithelium following H\textsubscript{2}S exposure; (c) developing a hybrid Physiologically-Based Pharmacokinetic - Computational Fluid Dynamic (PBPK-CFD) model for rats and humans; and (d) examining whether cytochrome oxidase inhibition in the nasal epithelium can be used as a tissue dosimeter. Research derived from these studies has supported derivation of a mechanistically-based inhalation reference concentration for this gas and improved our understanding of the mode of action of this chemical.

Implications: Hydrogen sulfide (H\textsubscript{2}S) fumes have a distinctive rotten-egg smell. Rats inhaling H\textsubscript{2}S develop specific lesions in regions of their noses. These lesions have been used by the US EPA to establish exposure guidelines for the general public. These exposure guidelines require regulators to estimate the amount of H\textsubscript{2}S that is delivered to similar regions in the human nose. We have completed a series of studies in rats to guide development of a state-of-the-art computer model to estimate H\textsubscript{2}S exposures needed to produce nasal toxicity in humans. Our model is now being used to generate exposure guidelines for this gas.

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Presentations:


**Peer-reviewed publications:**


This abstract was prepared by the principal investigator for the project. Please see [www.americanchemistry.com/lri](http://www.americanchemistry.com/lri) for more information about the LRI.
Other publication(s): None to date.


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