

Inhalation Toxicity of Brevetoxin 3 in Rats Exposed for Twenty-Two Days

Janet M. Benson,¹ Fletcher F. Hahn,¹ Thomas H. March,¹ Jacob D. McDonald,¹ Andrea P. Gomez,¹ Mohan J. Sopori,¹ Andrea J. Bourdelais,² Jerome Naar,² Julia Zaias,³ Gregory D. Bossart,⁴ and Daniel G. Baden²

¹Lovelace Respiratory Research Institute, Albuquerque, New Mexico, USA; ²Center for Marine Science Research, University of North Carolina at Wilmington, Wilmington, North Carolina, USA; ³Department of Pathology, University of Miami, Miami, Florida, USA; ⁴Division of Marine Mammal Research and Conservation, Harbor Branch Oceanographic Institution, Ft. Pierce, Florida, USA

Abstract

Brevetoxins are potent neurotoxins produced by the marine dinoflagellate *Karenia brevis*. Exposure to brevetoxins may occur during a *K. brevis* red tide when the compounds become aerosolized by wind and surf. This study assessed possible adverse health effects associated with inhalation exposure to brevetoxin 3, one of the major brevetoxins produced by *K. brevis* and present in aerosols collected along beaches affected by red tide. Male F344 rats were exposed to brevetoxin 3 at 0, 37, and 237 $\mu\text{g}/\text{m}^3$ by nose-only inhalation 2 hr/day, 5 days/week for up to 22 exposure days. Estimated deposited brevetoxin 3 doses were 0.9 and 5.8 $\mu\text{g}/\text{kg}/\text{day}$ for the low- and high-dose groups, respectively. Body weights of the high-dose group were significantly below control values. There were no clinical signs of toxicity. Terminal body weights of both low- and high-dose-group rats were significantly below control values. Minimal alveolar macrophage hyperplasia was observed in three of six and six of six of the low- and high-dose groups, respectively. No histopathologic lesions were observed in the nose, brain, liver, or bone marrow of any group. Reticulocyte numbers in whole blood were significantly increased in the high-dose group, and mean corpuscular volume showed a significant decreasing trend with increasing exposure concentration. Humoral-mediated immunity was suppressed in brevetoxin-exposed rats as indicated by significant reduction in splenic plaque-forming cells in both low- and high-dose-group rats compared with controls. Results indicate that the immune system is the primary target for toxicity in rats after repeated inhalation exposure to relatively high concentrations of brevetoxins. *Environ Health Perspect* 113:626-631 (2005).