

## **ROS-MEDIATED CYTOKINE EXPRESSION IN PINE-DUST EXPOSED RAT ALVEOLAR MACROPHAGES\***

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Respiratory symptoms, reduced lung function, and asthma have been reported in workers exposed to wood dust in a number of epidemiological studies. The underlying pathomechanisms, however, are not well understood. Pine is one of the most widely used wood species in the wood processing industry. In this study, the effects of dust from untreated pine (PD) and heat-treated pine (HPD) on the release of inflammatory mediators were analyzed in rat alveolar macrophages. After 4 h incubation, both PD and HPD induced a significantly ( $p < 0.05$ ) increased tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and macrophage inflammatory protein-2 (MIP-2) mRNA expression as well as a concentration-dependent (5 - 200  $\mu\text{g/ml}$ ) TNF- $\alpha$  and MIP-2 protein production. Interestingly, PD induced a significantly higher TNF- $\alpha$  and MIP-2 production than HPD. Polystyrene microspheres used as negative particulate control did not elicit a cytokine response. Moreover, a significantly increased reactive oxygen species (ROS) production, measured by dichlorofluorescein fluorescence, was observed in alveolar macrophages exposed to PD and HPD. In the presence of the antioxidants glutathione and N-acetyl-L-cysteine, the PD- and HPD-induced production of ROS, TNF- $\alpha$ , and MIP-2 was significantly reduced. Finally, electron spin resonance analyses demonstrated a significantly higher endogenous antioxidative capacity of HPD compared to PD. These results indicate that pine dust is able to induce an inflammatory response in rat alveolar macrophages and that ROS mediate the pine dust-induced TNF- $\alpha$ - and MIP-2 expression. Moreover, heat treatment of pine may improve the antioxidant ability of pine dust and thus reduce pine dust-induced inflammatory responses.

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