CORRELATION OF *IN VITRO* AND *IN VIVO* PULMONARY RESPONSES TO DIFFERENT CELLULOSE MATERIALS

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Abstract

In vitro studies were conducted with bleached cellulose pulp (BC), microcrystalline cellulose (MC) and cellulose insulation derived from recycled newsprint (CI). The *in vitro* responses were then compared to markers of pulmonary response for the same three materials after intratracheal instillation in rats. Immortalized rat alveolar type II epithelial cells (RLE-6TN) and alveolar macrophages (NR8383) were dosed with varying concentrations and for different periods of time, to create dose-response and time-response curves for the end points of LDH, pro-inflammatory and anti-inflammatory cytokines. TiO2, SiO2 and asbestos, were also studied in these two *In vitro* systems to provide comparisons with responses seen with nuisance and fibrogenic particulate materials. The *In vivo* studies in rats ranked the overall toxicity of these three cellulose materials as CI>MC>BC, as determined by analysis of biochemical markers, differential cell count and histopathology. Bronchial alveolar lavage samples (BAL) were analyzed for LDH, lysosomal acid hydrolases, alkaline phosphatase, total protein, and cell differentials at 3, 7, 14, and 28 days after dosing. The measures of response for the three different cellulose materials as determined in the *in vitro* systems provided an accurate representation of the responses determined *in vivo*, with the strongest association between lung enzyme responses and proinflamatory cytokines. Conversion of *in vitro* doses of the three cellulose materials to that used in the *in vivo* studies, based on ug/m3, indicated the degree of response in the different measured parameters as being of similar magnitude at approximately the same *in vitro* versus *in vivo* doses. With further exploration of these *in vitro* techniques, the mechanisms of response for some materials depositing in the lung may be determined, as well as providing tools for the better design of *in vivo* pulmonary experiments.

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