Title *

Biologic potency of diesel exhaust derived organic extracts, evaluated by calcium meassurements

Abstract *

The toxicity of diesel exhaust particulates (DEP) has been attributed to the complex mixture of adhered organic chemicals (OCs). However, the active substances remain to be identified.

The intracellular calcium level is kept low in the resting state, but functions as a central second messenger in a magnitude of cellular responses, including regulation of pro-inflammatory genes.

OCs were extracted and fractionated according to polarity from DEP (MAPCEL soot) by sequential extraction solvents (nonpolar → polar). Total OC and chemical composition was analyzed by Thermal Optical Analysis and GC-FID-MS. The potential of the extracted fractions to increase intracellular calcium was tested in HMEC-1 microvasculature endothelial cells. The role of the Ah-receptor (AhR) was explored by inhibitor (CH223191) and siRNA knock down. To classify the calcium results, cells were exposed in calcium free medium and the calcium-channel blockers SKF96365 and BtP2.

The two most lipophilic fractions (n-Hexane and DCM) stimulated increases in intracellular calcium levels in HMEC-1 cells. These two fractions also appeared to contain the majority of PAHs. The calcium response of both fractions depended on the aryl hydrocarbon receptor. While the DCM induced calcium seemed to be caused by extracellular calcium alone, the initial response to n-Hexane came from an intracellular source, probably the endoplasmic reticulum.

To link these calcium responses to inflammation, cells were treated with SKF96365 and then exposed to the lipophilic fractions. Both n-Hexane and DCM induced COX-2 at 5 hours, but only the DCM mediated response was inhibited by SKF96365.

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