HEPMEAP: *In vitro* and *in vivo* toxic potency of ambient fine and coarse PM across Europe: the influence of traffic exhaust emissions

Miriam E. Gerlofs-Nijland, John F. Boere, Ingeborg M. Kooter, Daan L.A.C. Leseman, Jan A.M.A. Dormans, Ken Donaldson, Ian Mudway, Cecilia Gustadisegni, Henk J.T. Bloemen, Leendert van Bree and Flemming R. Cassee

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Introduction

Ambient particulate matter (PM) may be responsible for serious respiratory and cardiovascular health effects or even premature mortality especially among susceptible sub-populations. To assess the inflammatory and toxic potential of ambient suspended particles collected at places across Europe with contrasts in traffic intensity and to link these properties with chemical composition data on the one hand and epidemiological health observations on the other hand, different EU PM samples fine (PM0.1-2.5) and coarse (PM10-2.5) were tested *in-vitro and in-vivo* (both rats and humans).

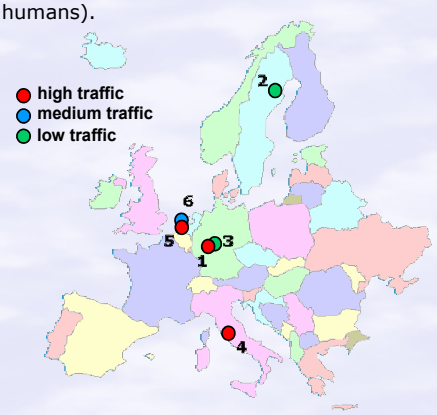

Figure 1: Site selection for *in vivo* study.

1 - D, Ostbahnhof; **2** - S, Lycksele; **3** - D, Grosshadern; **4** - I, Rome; **5** - NL. HIA; **6** - NL, Dordrecht.

To choose a selection of the EU PM samples for the *in-vivo* study, samples were ranked based on ascorbate depletion, arachidonic acid release, IL-6, and DNA damage (Table 1). Furthermore the site selection (Figure 1) and chemical characterization were taken into account. The most interesting samples were selected based on 4 categories (most or least reactive in both fractions and greatest contrast between fractions with fine or coarse most reactive).

Materials and Methods

Spontaneous hypertensive rats (SHR; 12-weeks-old) received a single PM dose (3 or 10 mg PM per kg bodyweight). Health effects were determined at 24 hours after this treatment using lung histopathology, bronchoalveolar lavage fluid and blood analysis.

Results

PM site	*In vitro* ranking results
1	high ascorbate, AA release, DNA damage; mainly coarse
2	high AA release, IL-6;mainly fine - high hop/ster/V/B(a)P;coarse/fine
3	high ascorbate, IL-6;mainly fine - low hop/ster/V/B(a)P;coarse/fine
4	high AA release;coarse/fine - high Ni/Cu/Zn;coarse/fine
5	high AA release, IL-6;coarse/fine
6	high ascorbate, IL-6;mainly coarse

Table 1: *In vitro* ranking results

Figure 2 shows a marked, dose-dependent increase in cytotoxicity (LDH), the coarse fraction being more potent than the fine fraction. All samples induced increased lung permeability (albumin) with the exception of the sample from Rome.

In general, exposures to PM lead to an dose dependent oxidative stress response (anti-oxidants such as glutathione and uric acid) (Figure 3).

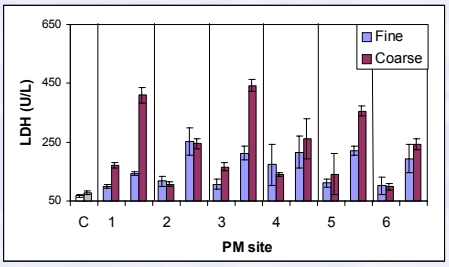

Figure 2: LDH concentrations in BALF of SHR exposed to saline control (C) or EU PM samples at 24 hrs after a single intratracheal instillation of 3 respectively 10 mg/kg bodyweight. Values are presented as means ± standard errors of the mean, *N*=7-8

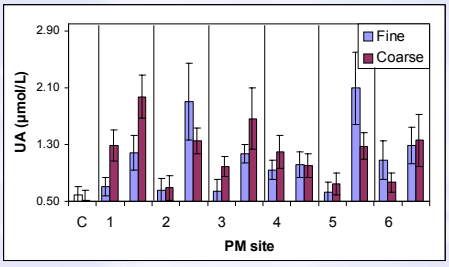

Figure 3: Example of a anti-oxidant induction in BALF of SHR at 24 hrs post-exposure.

Significant inflammatory response were observed as indicated by an increased neutrophil-influx (Figure 4) and increased cytokine levels in the lungs. This effect was most prominent for coarse fraction PM whereas fine resulted primarily in increased macrophages (Figure 5) showing an increased host defense.

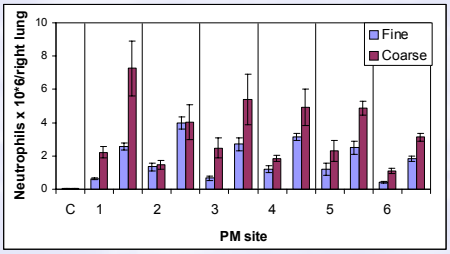

Figure 4: Neutrophil concentration in BALF of SHR at 24 hrs post-exposure.

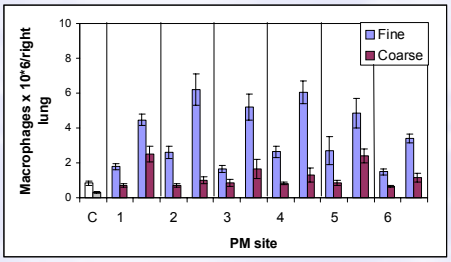

Figure 5: Macrophage concentration in BALF of SHR at 24 hrs post-exposure.

Particularly the PM sampled in Germany at the Ostbahnhof and the HIA PM from the Netherlands show severe pathological changes. Both these samples and the PM from Grosshadern also resulted in increased cell proliferation compared to the other samples.

Conclusions

The still incomplete database of results indicate that

- All selected ambient fine and coarse PM samples express toxic potency.
- PM from locations with a high density of road traffic induce more effects than those from low density traffic areas.
- Both coarse and fine PM fractions induce adverse health effects, but affect different indicators.
- The correlation between *in vitro* data and *in vivo* outcomes has not yet been studied.

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More information at WWW.HEPMEAP.ORG