Assessment of Diesel exhaust particulate exposure and surface characteristics in association with levels of oxidative stress biomarkers

Exposure to PM_{10} and $PM_{2.5}$ (particulate matter with aerodynamic diameter smaller than 10 μm and 2.5 μm, respectively) is associated with a range of adverse health effects, including cancer, pulmonary and cardiovascular diseases. Surface characteristics (chemical reactivity, surface area) are considered of prime importance to understand the mechanisms which lead to harmful effects. A hypothetical mechanism to explain these adverse effects is the ability of components (organics, metal ions) adsorbed on these particles to generate Reactive Oxygen Species (ROS), and thereby to cause oxidative stress in biological systems (Donaldson et al., 2003). ROS can attack almost any cellular structure, like DNA or cellular membrane, leading to the formation of a wide variety of degradation products which can be used as a biomarker of oxidative stress.

The aim of the present research project is to test whether there is a correlation between the exposure to Diesel Exhaust Particulate (DEP) and the oxidative stress status. For that purpose, a survey has been conducted in real occupational situations where workers were exposed to DEP (bus depots).

Different exposure variables have been considered:

- particulate number, size distribution and surface area (SMPS);
- particulate mass - $PM_{2.5}$ and PM_4 (gravimetry);
- elemental and organic carbon (coulometry);
- total adsorbed heavy metals - iron, copper, manganese (atomic adsorption);
- surface functional groups present on aerosols (Knudsen flow reactor). (Demirdjian et al., 2005).

A biomarker of oxidative stress (8-hydroxy-2'-deoxyguanosine) has been determined in urine of volunteers.

Results obtained during the sampling campaign in several bus depots indicated that the occupational exposure to particulates in these places was rather low (40-50 $\mu g/m^3$ for PM_4). Bimodal size distributions were generally observed (5 μm and <1 μm). Surface characteristics of PM_4 varied strongly, depending on the bus depot. They were usually characterized by high carbonyl and low acidic sites content. Urinary levels of 8-hydroxy-2'-deoxyguanosine increased significantly ($p<0.05$) during two consecutive days of exposure, only for non-smoker workers.

Biomarkers levels will be compared to exposure variables to gain a better understanding of the relation between the particulate characteristics and the formation of ROS by-products.

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Donaldson K., Stone V., Borm P. J., Jimenez L. A., Gilmour P. S., Schins R. P., Knaapen A. M., Rahman I., Faux S. P., Brown D. M., MacNee W., 2003. *Free Radical Biol. Med.*, 34, 1369-1382.

Assessment of Diesel Exhaust Particulate exposure and surface characteristics in association with levels of oxidative stress biomarkers

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1. INTRODUCTION

- Particulate Matter (PM) exposure is associated with a range of adverse health effects. **Surface characteristics** (reactivity, area) are of prime importance to understand the mechanisms which lead to harmful effects.
- The most important mechanism to explain these adverse health effects is the ability of some components (organics, metal ions) adsorbed on these particles to induce **oxidative stress** (Fig. 1).
- **8-hydroxy-2'-deoxyguanosine** (from oxidative DNA damage) may be considered as **oxidative stress biomarker**.
- Increase of **oxidative stress** has been found to induce **anti-oxidant defenses** (A. Nel et al., *Science*, 311, 622-627, **2006**).

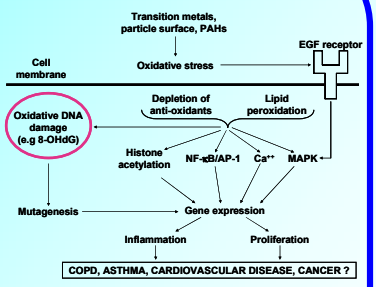


Fig. 1 : Simplified diagram of hypothetical oxidative stress-mediated effects of PM_{10} leading to adverse health effects (K. Donaldson et al., *Free Radical Biology and Medicine*, 34 (11), 1369-1382, **2003**).

2. OBJECTIVE OF THE RESEARCH

Is there a correlation between the exposure to Diesel Exhaust Particulate (DEP) and the oxidative stress status?

To answer this question, a survey has been conducted in real occupational situations, where workers were exposed to DEP and possibly to other ambient aerosols (bus depots) :

- Selection of a homogeneous group of DEP exposed workers ;
- Urine and serum sampling during two consecutive days of exposure ;
- Assessment of the exposure to DEP through stationary and personal samplings ;
- Quantification of oxidative stress biomarker and levels of anti-oxidants in urine of volunteers.

3. MATERIALS AND METHODS

- Particles have been sampled in several bus depots (maintenance yards) in Switzerland by means of two **High-Volume Samplers** equipped with silanized quartz fiber filters.

Exposure variables :

- Particulate number, size distribution and surface (**Scanning Mobility Particle Sizer**) ;
- Particulate mass – PM_4 (**gravimetry**) ;
- Elemental and organic carbon (**coulometry**) ;
- Surface functional groups present on particles (**Knudsen flow reactor**, Fig. 3) ;
- Total adsorbed heavy metals (**Atomic Absorption**) ;
- NO_x and ozone concentrations (**direct reading instruments**).

Biological effects :

- **8-hydroxy-2'-deoxyguanosine** in urine (clean-up by **SPE**, analysis by **LC/MS-MS**) ;
- Level of **anti-oxidants** in urine (method by **EDEL Therapeutics**)

Fig. 2 : Picture of a sampling site (bus depot, maintenance yard).

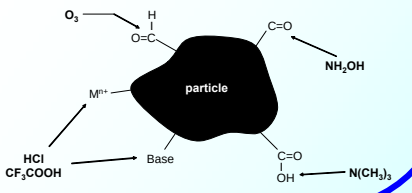
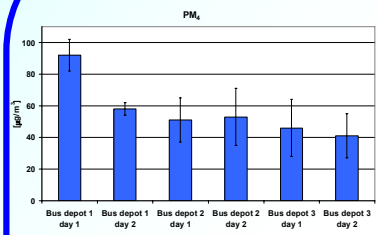
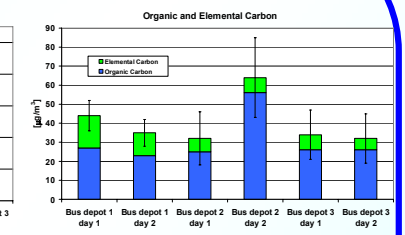


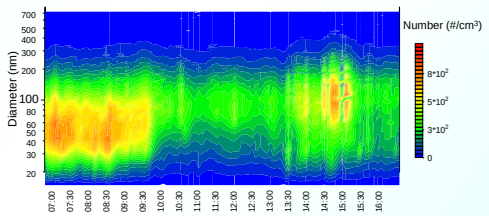
Fig. 3 : Schematic drawing of the heterogeneous chemical reactions occurring during the titration experiments in the **Knudsen flow reactor**, allowing to measure the density of functional groups present on the surface of the particles.

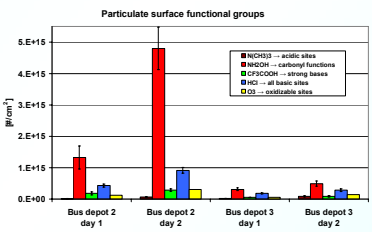
4. RESULTS

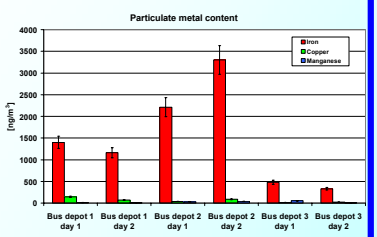
Exposure characterization (stationary sampling) :



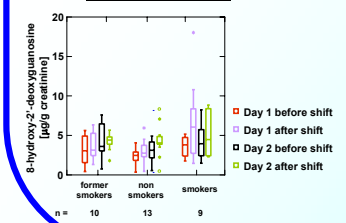


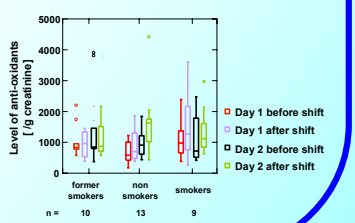






Biological effects :





5. DISCUSSION

Exposure characterization :

- Exposure to particulate matter was low.
- Number size distribution shows particles mostly in the submicron range.
- PM_4 were mainly carbon-based (Diesel and ambient particles).
- Surface functional groups of sampled particles were very different between the bus depots.
- Surface functional groups of sampled particles were usually characterized by high carbonyl and low acidic sites content.
- Particulate iron content was clearly higher than copper and manganese.

Biological effects :

- Urinary levels of 8-hydroxy-2'-deoxyguanosine were **higher for smokers** than for non-smokers (day 1 before shift).
- Urinary levels of 8-hydroxy-2'-deoxyguanosine increased significantly during two consecutive days of shift, **only for non-smokers**.
- The increase of the oxidative stress biomarker for non-smokers was associated with an increase of the level of anti-oxidants.

6. CONCLUSION

Working in bus depots increased oxidative damages on DNA for non-smokers, although exposure to PM was low. This oxidative stress induced biological response through an increase of the level of anti-oxidants. Causal parameters of oxidative stress are not yet identified, but statistic evaluations are ongoing.

7. ACKNOWLEDGMENTS

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COST ACTION 633
Particulate Matter
Properties Related to Health Effects

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