

Title of the project		
Effects of PAHs in environmental pollution on exogenous and endogenous DNA damage		
Acronym of the project		
EXPAH		
Type of contract		Total project cost
Shared-cost		€ 1.221.863
Contract number	Duration	EU contribution
QLK4-CT-2000-00091	39 Months	€ 998.499
Commencement date	Period covered by the progress report	
1 January, 2001	1 January 2003 – 31 March 2004	
<u>PROJECT COORDINATOR</u>		
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Key words		
PAHs, environmental pollution, DNA damage, polymorphism, biomarkers		
World wide web address		
http://www.le.ac.uk/biochem/pbf1/EXPAH.html		
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Objectives:

The main objectives of this programme were as follows:

1. To evaluate the hypothesis that PAHs are the major source of the genotoxic activities of organic mixtures associated with air pollution. The sensitivity of all biomarkers used will be checked in four different populations with different level of PAHs exposure.
2. To evaluate the relationship between endogenous and oxidative DNA damage in a human population exposed to PAHs. A population exposed to a high level of environmental pollutants (e.g. PAHs and their derivatives) will be included.
3. To study the effect of metabolic polymorphisms and DNA repair genotypes on biomarkers of exposure and effect.
4. To evaluate the impact of diet on endogenous DNA damage. This will include assessment of dietary exposures to PAHs and smoking.
5. To use *in vitro* systems using human cells for studying the genotoxic effect of the complex mixture of organic compounds that are adsorbed to air particles in each locality studied.
6. To assess the risk caused by exposure to carcinogenic PAHs from environmental exposure in each locality studied, based on *in vitro* and human studies.

Results and Milestones:

The project was completed with the following milestones.

1. Establishment of the study protocol (month 6)
2. Standardisation of the methods among laboratories. Samples have been exchanged between laboratories (month 6).
3. Human sample collection and distribution. Blood and urine samples have been collected from 350 human volunteers in Czech Republic, Slovakia and Bulgaria (month 14).
4. Air monitoring. The characterisation of the air pollution has been achieved in each country, and organic matter extracted and distributed (month 24).
5. Cell systems have been established and used to study the response of human cells to the complex mixtures (extracts of organic compounds associated with PM10). Biomarkers of exposure and effect have been examined (month 27).
6. Biomarkers of exposure, effect, susceptibility and oxidative damage have been determined in the human biological samples, and compared with environmental exposure to PAHs. Susceptibility of human cells to oxidative damage was also estimated after X-ray irradiation (month 33).
7. The biomarker data have been statistically appraised for the evaluation of PAHs in environmental exposure for risk assessment (month 39).

The results indicate that PM10 levels were higher in winter compared to summer in all three locations. Extractable organic matter per PM10 was at least 2 fold higher in winter than summer. Concentration of carcinogenic PAHs was at least 10 fold higher in winter than summer. In Prague and Sofia, the exposed group had about twice the exposure of controls, and in Kosice, the exposed group had about three times the exposure of controls. For the whole population, total bulky DNA adducts and B(a)P DNA adducts were significantly more abundant in the exposed group compared to the control group, and in smokers compared to non-smokers. Total and B(a)P DNA adducts were highly statistically correlated, as was 8-oxodG (negative correlation) with total and B(a)P DNA adducts. Changes in oxidative DNA damage products were observed at statistical significance between the exposed and control groups for 8-oxodG in Kosice and M₁dG in Sofia. The country of origin of the samples was associated with total DNA adducts, and B(a)P adducts levels, independently from other possible confounding factors. FISH was more sensitive than conventional cytogenetic methods as a biomarker of effect. An independent effect of age and exposure on FISH was observed. GSTP1 polymorphism was significantly associated with FISH. Ambient air exposure increased cytogenetic parameters in non-smokers. Genetic polymorphism of GSTM1 affected the B(a)P adduct in the whole population. Effects of polymorphisms of GSTT1, CYP1A1, and XPD repair gene were seen on some biomarkers of exposure or effect, or of oxidative damage, in subgroups from individual countries. Vitamin A levels were significantly negatively correlated with M₁dG, total and B(a)P DNA adducts, and vitamins E and C with total and B(a)P DNA adducts. Significant location and season-related differences were found in the ambient air genotoxicity measured in cellular systems, when expressed in terms of the EOM content/ m³ air. Environmental exposure to PAHs significantly influenced the repair process of DNA damage induced by X-rays in the subject's lymphocytes.

Benefits and Beneficiaries:

The quality of life of the EU citizen would be enhanced if environmental health hazards could be reduced. As a particular example, it is important to ascertain if cancer incidence could be decreased by improvements in our environment. A very appropriate way to approach this question is to explore cause: effect relationships for carcinogenesis by the study of DNA damage in exposed populations. The aim of this project was to propose methods of molecular epidemiology for the risk assessment of PAH exposure in air, and to check if there are any susceptible populations to PAHs according to their genotypes.

The work has shown the biomarkers of choice for exposure and effect monitoring and has demonstrated some influences of individual genotypes. This information should guide future environmental pollution studies, designed to achieve a reduction in genotoxic damage by reduction of pollution and/or change of lifestyle, which will ultimately result in a decrease in human cancer incidence.

Future Actions (if applicable):