5. Summary and Conclusions

In vitro studies

- Cell-free system in conjunction with the sensitive ^{32}P- postlabelling is a suitable approach to detect genotoxic potential of EOMs, particularly those containing c-PAHs, as well as to distinguish between direct and indirect genotoxicants in the complex mixtures of environmental pollutants.
- HepG2 cells are an appropriate *in vitro* model to test genotoxic potential of complex mixtures since they are metabolically competent to activate c-PAHs as the most important genotoxic EOM components and yield dose-response relationship of adduct forming activity in a wide range of EOM concentrations.
- HEL cells are sensitive enough to detect DNA adducts of individual c-PAHs, but strong toxicity occurs when artificial c-PAH mixtures and real EOMs are employed.
- DNA adduct patterns derived from the different localities and sampling periods resemble each other. This fact suggests that the spectra of genotoxic EOM components in studied cities are similar.
- c-PAHs contribute predominantly to the total genotoxicity of various EOMs.
- B[a]P is of outstanding importance as a reference c-PAH for many environmental complex mixtures and may be used as the indicator of c-PAH concentrations and biological activity of these mixtures.
- The estimation of the genotoxic potential of ambient air and prediction of health risk should be based preferably on c-PAH concentrations.

Human epidemiological study

- DNA adduct levels were not associated with the individual metabolic and DNA repair gene polymorphisms, but correlation was found with combinations of genes, encoding enzymes, primarily involved in c-PAH metabolism, under conditions of increased exposure to c-PAHs.
- Concentration of 1 ng B[a]P /m^3 of the ambient air seems to be critical, and its exceeding can lead to exhaustion of DNA repair capacity and increased level of DNA adducts in human tissues.

- DNA adducts in lymphocytes of subjects exposed to increased c-PAHs levels in polluted air are an appropriate biomarker of biologically effective dose, directly indicating whether or not the extent of exposure to these compounds is related to the increased mutagenic and carcinogenic risk.