

was doubled with co-exposure of thallium, PFOS, lead, cadmium, manganese, and mercury, while in boys the mixture of MECPP with cadmium showed the strongest association with birth weight. In conclusion, birth weight was consistently inversely associated with exposure to pollutant mixtures. Chemicals not showing significant associations at single pollutant level contributed to stronger effects when analyzed as mixtures

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#### P24-002

##### The hematotoxicity of Cd and PCBs mixture: Employing the rat experimental model to evaluate the effects on blood cells count



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Humans are concurrently and simultaneously exposed to hundreds of thousands of chemicals from very different sources, hence the exposure assessment and toxicological evaluation should be focused on mixtures rather than on single chemicals, giving special attention to potential interactions between chemicals in mixtures. In this study, hematotoxicity of mixture of cadmium (Cd) and polychlorinated biphenyls (PCBs), widely spread persistent environmental pollutants, has been evaluated.

In order to assess the potential hematotoxicity of this “cocktail of pollutants”, Wistar rats were subacutely orally treated with six different doses of single chemicals or nine different dose combinations of their mixtures. Blood samples were collected from carotid artery and red blood cells (RBC), white blood cells (WBC) and platelets (PLT) were counted. Statistical significance differences among data were tested using ANOVA+ Fisher's LSD test while possible interactions were assessed using the concept of differences in slope of dose–response curves for single chemicals and for mixture.

Results of this study showed that Cd and/or PCBs can induce adverse effects on hematopoietic system as one of the most sensitive systems in organism. Both single and mixture treatments produced statistically significant effects on WBC and PLT count; the effects of mixtures were shown to be additive. Furthermore, mixtures produced significant decrease in RBC count when compared to controls, although this effect was not observed during the same dose regime of single components.

These results implicate that mixture can exert toxic effects that are not induced by their single components indicating complexity of risk assessment of mixtures.

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#### P24-003

##### Effects of a mixture of two cyanobacterial toxins (microcystin-LR and L-BMAA) on spatial learning and memory in adult C57BL/6 mice



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The cyanobacterial toxins  $\beta$ -Methylamino-L-alanine (L-BMAA) and microcystin-LR (MC-LR) are suspected to cause human neurological diseases. MC-LR is in addition a potent liver toxin. Here, male adult C57BL/6J OlaHsd mice (ex-breeders) aged approximately 11 months were treated with L-BMAA and microcystin-LR alone, or in combination, for five consecutive days by subcutaneous administration. A dose-range study determined a tolerable daily dose of 30  $\mu$ g MC-LR/kg BW. The L-BMAA (not acute toxic) dose and latency time was based upon published results from others. Thus, the mice were given 30  $\mu$ g MC-LR/kg BW and/or 30 mg L-BMAA/kg BW, either alone or in mixture for five consecutive days. Cumulative doses were 150  $\mu$ g MC-LR/kg BW, 150 mg L-BMAA/kg BW, or 150  $\mu$ g MC-LR/kg BW + 150 mg L-BMAA/kg BW. No deaths occurred. After 4 weeks, spatial learning and memory performance of the mice was compared to control mice for three days (six sessions) using a Barnes maze with video tracking. The mice were also re-tested for long-term memory effects 10 weeks after exposure on one day (two sessions). Several parameters (box escape latency time, number of errors, start-angle error, etc.) were evaluated and will be presented.

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#### P24-004

##### Genotoxic potential of the binary mixture of cyanotoxins microcystin-LR and cylindrospermopsin



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The blooming of cyanobacteria is associated with the production of hazardous cyanotoxins. The most studied cyanotoxin, microcystin-LR (MCLR) is classified as possible human carcinogen, while cylindrospermopsin (CYN) has only recently been recognized as health concern. Both cyanotoxins are ubiquitously and simultaneously present in freshwater environment. It is known that they are genotoxic; however, the mechanisms of their toxicity differ.

As it is known that adverse effects of complex mixtures can be more pronounced compared to individual compounds, genotoxic potential of binary mixture of MCLR and CYN was studied. Human hepatoma HepG2 cells were exposed to non-cytotoxic graded doses of CYN (0.01–0.5  $\mu$ g/mL), single dose of MCLR (1  $\mu$ g/mL) and their combinations for 4 and 24 h and subsequently DNA damage was assessed with the comet and cytokinesis-block micronucleus cytome assay. In addition, mRNA expression of genes involved in xenobiotic metabolism, immediate/early response, and DNA-damage response were studied with qPCR. MCLR (1  $\mu$ g/mL) did not induce DNA damage, while CYN (0.5  $\mu$ g/mL) significantly increased