# Project summary

Humans are long life exposed to a significant number of chemicals, primarily as a consequence of environmental pollution as well as occupationally.

Our research project is directed to investigation of toxic metals and minerals: cadmium (Cd), lead (Pb), mercury (Hg), fluoride (F-), persistent organic pollutants: polychlorinated biphenyls (PCB) and polybrominated diphenyl ethers (PBDE) and pesticides: organochlorines and organophosphorus compounds, as well as their mixtures.

Examination of toxicity mechanisms that are under our objectives include evaluation of the influence of chemicals on enzyme activities, hormone homeostasis, interactions between toxic substances and bioelements, influence on oxidative stress and antioxidative defense system. Critical toxic effect assessment is of utmost interest for human health risk assessment and represents analysis of points of departure and health based guidance values (i.e. Benchmark dose – BMD) linked to target tissue damages.

Under the frame of the project is also investigation of antidotal efficacy of the two novel oximes, K027 and K203, that can be potentially used in human medicine in the treatment of acute organophosphate poisonings.

Particularly important are those project tasks focused to establish the relationship between exposure to the toxic substances and endocrine disruption, as well as between exposure and carcinogenesis and tumor development. Concerning the specific outcome, along with animal experiments, project activity is monitoring of exposure levels to toxic substances in humans as one of risk factors for the development of certain disease.

Keywords**:** toxic metals and minerals, persistent organic pollutants, pesticides, mechanisms of toxicity, antidotal efficacy of K203 and K027, mixture toxicity, interactions, Benchmark dose (BMD), critical toxic effect

# Sažetak projekta

Ljudi su celoživotno izloženi značajnom broju toksičnih jedinjenja, primarno kao posledica zagađenja životne sredine, ali i usled profesionalne ekspozicije.

Istraživanja našeg tima usmerena su na ispitivanja toksičnosti metala i mineralnih otrova: kadmijumu (Cd), olovu (Pb), živi (Hg), fluoridima (-F-), perzistentnih organskih zagađivača: polihlorovanih bifenila (PCB) i polibromovanih difeniletara (PBDE) i pesticida: ogranohlorna i organoforsforna jedninjenja, kao i njihovih smeša. Mehanizmi toksičnosti koje istražujemo obuhvataju dejstvo na enzimsku aktivnost, homeostazu hormona, interakcije toksičnih supstanci sa bioelemenatima, uticaj na oksidativni stres i antioksidativnu zaštitu. Procena kritičnog toksičnog efekta je od primarnog interesa za procenu rizika po zdravlje ljudi i uključuje analizu odgovarajućih doznih nivoa (Benchmark doza- BMDL) koji dovode do poremećaja funkcije I građe ciljnih organa i tkiva.

U okviru projekta se ispituje i antidotska efikasnost novosintetisanih bispiridinijumskih oksima K027 i K203, usmerena ka njihovoj potencijalnoj upotrebi u humanoj medicini za terapiju trovanja organofosfornim jedinjenjima.

Od posebnog značaju su ona istraživanja koja su u funkciji iznalaženja veze između izloženosti toksičnim supstancama i poremećaja endokrine funkcije, kao i karcinogeneze i pojave malignih oboljenja. U tom cilju, pored istraživanja na eksperimentalnim životinjama, kao oblast projekta sprovode se I praćenja nivoa izloženosti toksičnim supstancama kod ljudi kao jednog od faktora rizika za razvoj određenog oboljenja.

Ključne reči: toksični metali i mineralni otrovi, perzistentni organski zagađivači, pesticidi, mehanizmi toksičnosti, antidotka efikasnost oksima K027 i K203; toksičnost i smeša, interakcije, Benchmark doza (BMD), kritični toksični efekti

# Selected results/Odabrani rezultati

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