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P308-034
Recent genetic damage in a pesticide-exposed population: Comet assay and micronuclei in reticulocytes

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A wide range of chemical products known to be acutely toxic are used nowadays in the agricultural sector. Nevertheless, the effects in human health as result of long-term exposure to low levels are not yet completely understood. Scientific evidences have been showing the existence of associations between a few kinds of cancers and pesticide exposure. However information respecting the identification of chemical groups involved in those processes and possible synergisms between them is still scarce. DNA damage can be on the basis of several cellular alterations, some of them possibly leading to cancer. Both Comet assay and micronuclei in reticulocytes (MN-RET) provide information on recent genetic damage being therefore useful to characterize this kind of pesticides outcome.

Study population comprised 43 farmers working in the northern region of Portugal exposed to pesticides. Genetic damage was evaluated by Comet assay and MN-RET (using flow cytometry technique). A non-exposed group ($n = 73$) from the same area and with same demographic characteristics without exposure to genotoxic compounds was studied and data obtained from both groups was compared.

Pesticide-exposed individuals presented significantly increased DNA damage assessed both by Comet assay parameters and MN-RET frequency. Other variables such as time of exposure, age, gender, type of exposure (open-field and greenhouses) and smoking habits were also considered in statistical analysis and proven to be irrelevant to observed DNA damage levels. Timing of sampling appears to be important as increased DNA damage was found in samples collected during summer (within exposed group). This fact is probably due to intensive pesticide exposure during these months. A good correlation between all studied endpoints (MN-RET and different comet assay parameters: percentage of DNA in tail, tail length and tail moment) was observed.

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P308-035
Adaptive response of *Saccharomyces cerevisiae* UE-ME3 to isoproturon depends on the presence of peptone in the rich culture medium

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The isoproturon, a herbicide which acts as a photosynthesis inhibitor is consider by some authors as toxic to humans having ability for tumors induction. When this phenylurea is metabolized by biotransformation systems can generate oxidative stress, activating electron transport chains present at mitochondria and endoplasmic reticulum and causing an increase of intracellular ROS. Having in account exposure above, the main purpose of this work was to compare the effects of isoproturon on cell growth, glutathione level and catalase T (CAT), glutathione peroxidase (GPx), alcohol dehydrogenase (ADH) and lactate dehydrogenase (LDH) activities of *Saccharomyces cerevisiae* UE-ME3, wild-type strain of Alentejo, Portugal, growing in YEPD, YED and YEP media. Cells at mid-exponential phase were inoculated in each medium and incubated during 72 h in a water bath with orbital stirring, at 28 °C, in the absence or presence of 100 μM isoproturon. Samples from each treatment were used to obtain growth curves and to prepare post-12,000 × *g* supernatant, used for determination of GSH level as well as CAT T, GPx, ADH and LDH activities. The results show that isoproturon cause a significant increase of cell survival, GSH/GSSG ratio, LDH activities in yeast growing in presence of peptone plus glucose or peptone. Despite, isoproturon cause a decrease of CAT T and GPx ability to scavenger H_2O_2 or lipid hyroperoxides, it was also observed an increase of ADH activity in all media tested. The maintenance of high levels of GSH, as well as, the dehydrogenases responses can be interpreted as a stress adaptive mechanism to isoproturon where ADH and LDH are crucial enzymes for cytosolic NAD + recycling.

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P308-036
Organophosphorus (OP)-hydrolyzing enzymes in OP antagonism: Cholinesterase inhibition as indicator of op intoxication

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Two organophosphorus (OP)-hydrolyzing recombinant enzymes, organophosphorus acid anhydrolase (OPAA) and organophosphorus hydrolase (OPH) were employed in combination with 2-PAM and atropine against paraoxon and diisopropylfluorophosphate (DFP) as model compounds for OP agricultural pesticides and chemical warfare agents, such as sarin and soman. This study suggests that acetylcholinesterase (AChE) activity can serve as an indicator of in vivo antidotal protection. Reactivation of the OP-inhibited AChE was proportional to the pralidoxime (2-PAM) concentration, and the AChE level was proportional to the concentrations of DFP or paraoxon and the OPAA or OPH, respectively, when the enzymes were nano-captured within polyoxazoline based dentritic polymeric nano-capsules (DP). These studies also compare the in vivo efficacy expressed as "Antidotal Potency Ratio" (LD50 of paraoxon or DFP with the antagonists/ LD50 of paraoxon or DFP without the antagonists) of the two nano-captured enzymes as antidotal systems. The studies demonstrate a synergistic enhancement of the antagonistic therapies, since the antidotal protection of 2-PAM + atropine against DFP and paraoxon is approximately 8 and 60 × LD50, respectively. These studies represent a practical application of externally administered, nano-capsulated metabolizing enzymes in drug antidotal therapy.

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