

**P03-063****Mutagenicity and DNA repair of glycidol-induced adducts in mammalian cells and dose measurements using the cob(I)alamin trapping method**J. Aasa<sup>1,\*</sup>, D. Vare<sup>2</sup>, H.V. Motwani<sup>1</sup>, D. Jenssen<sup>2</sup>, M. Törnqvist<sup>1</sup><sup>1</sup> Stockholm University, Dept. of Environmental Science & Analytical Chemistry, Stockholm, Sweden<sup>2</sup> Stockholm University, Dept. of Molecular Biosciences, The Wennergren Institute, Stockholm, Sweden

Glycidol (Gly) is found as a food process contaminant in e.g. different refined edible vegetable oils. It has been extensively evaluated in *in vitro* and *in vivo* genotoxicity tests and has been shown to be an animal carcinogen. We have further evaluated the mutagenic potency of Gly in Chinese hamster ovary cell lines, CHO (wild-type cells and cells defective in base excision repair, BER) by using the HPRT assay. In addition, mechanisms involved in the DNA repair of Gly-induced adducts have been investigated by using CHO cell lines deficient in different repair mechanisms; base excision repair (BER), nucleotide excision repair (NER) or homologous recombination (HR) in comparison to wild-type cells. We have applied the alkaline DNA unwinding assay (ADU) for analysis of number of strand breaks related to different repair processes and the DRAG assay (detection of repairable adducts through growth inhibition) in order to map pathways involved in the repair of Gly-induced DNA lesions. Gly is electrophilically reactive which means that it has a short half-life in cells. Thus the accurate quantification of the dose during treatment of cells is difficult. By introducing the *in vitro* trapping agent cob(I)alamin, which forms a stable reaction product with Gly, we have been able to measure the concentration of Gly in the cell cultivation medium. This enables a true estimate of the dose over time (mMh), which is required for determination of the mutagenic potency. It was concluded that the concentration of Gly in the medium was relatively stable during the treatment time in the assays. We have shown that Gly is a cytotoxic compound which gives a weak but significant mutagenic effect of the *hprt*-gene both in the wild-type cells and the BER deficient cells, with mutagenic potencies of  $0.08 \pm 0.01$  mutants/ $10^5$  cells/mMh and  $0.20 \pm 0.05$  mutants/ $10^5$  cells/mMh, respectively. In addition Gly causes strand breaks due to repair incisions which are repaired by the involvement of several repair systems but mainly dependent on the short patch BER system. Gly also causes a dose dependent stalled replication fork elongation, independently of repair mechanism. The obtained result is compared to the mutagenic potency of other structurally similar compounds, and will be part of a larger dataset aiming to evaluate methods for cancer risk estimation.

<http://dx.doi.org/10.1016/j.toxlet.2015.08.352>**P03-064****Antipsychotics but not electromagnetic field influence the process of neurogenesis in the brains of adult rats**R. Wiaderkiewicz<sup>1,\*</sup>, A. Pałasz<sup>1</sup>, E. Gołębiewska-Rojczyk<sup>1</sup>, A. Suszka-Switek<sup>1</sup>, K. Bogus<sup>1</sup>, Ź. Filipczyk<sup>1</sup>, J. Karpowicz<sup>2</sup><sup>1</sup> Medical University of Silesia, Histology & Embryology, Katowice, Poland<sup>2</sup> Central Institute For Labour Protection – National Research Institute, Warsaw, Poland

Adult neurogenesis in the mammalian brain is well established phenomenon and any chemical or physical environmental factors that affect this process may have important clinical consequences. In our study adult Wistar Rats were injected for 28 days with olanzapine, chlorpromazine or haloperidol (daily i.p. injection, 2 mg/kg b.w.) or were exposed to electromagnetic field, EMF (7 h daily, 3 levels of exposure: 1370 mT, 100 V/m; 78 mT, 10 V/m; or 10 mT, 7 V/m). Neurogenesis was assessed immunohistochemically in different brain areas by staining the brain tissue sections with anti Ki67 and anti doublecortin (DCX) antibodies. Gene expression of selected neurotrophic factors (POMC, NPY and their receptors) as well as caspase 3, as marker of apoptosis, were also measured on mRNA level by RT-PCR method. The obtained results indicate that long term (28 days) treatment of rats with studied neuroleptics modulates the neurogenesis in the brain of adult animals and the effect could be both stimulatory (olanzapine, chlorpromazine) or inhibitory (haloperidol). What is interesting, we have shown that the process of neurogenesis occurs, and is affected, not only in the classical niches like subgranular zone of hippocampal dentate gyrus and subventricular zone of lateral ventricles but also other brain regions like hypothalamus – the area extremely important for the regulation of many metabolic functions in the whole organism. Slight changes in the neurogenesis level (DCX positive cells) observed after exposure of rats to EMF were, in the analyzed exposure range, statistically not significant. Staining of the brain sections by Nissl method or immunohistochemically with anti-caspase 3 antibody show that none of the studied antipsychotics nor EMF induce any neurodegenerative changes in the conditions of performed experiment.

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<http://dx.doi.org/10.1016/j.toxlet.2015.08.353>**P03-065****Climate changes and mycotoxins: Two risk factors associated**S. Viegas<sup>1,2,\*</sup>, M. Meneses<sup>1</sup>, C. Viegas<sup>1,3</sup><sup>1</sup> ESTeSL-IPL, Environmental Health, Lisboa, Portugal<sup>2</sup> Centro de Investigação em Saúde Pública (CISP/ENSP/UNL), 1600-560, Lisbon, Portugal, Portugal<sup>3</sup> Environmental Health Institute–Faculty of Medicine from Lisbon University, Lisbon, Portugal, Portugal

Many species of fungi produce bioactive compounds called mycotoxins. These compounds are produced by filamentous fungi

and can contaminate food, feeds and specific indoor environments resulting in high economic losses. Severe health problems and death have been related with mycotoxins exposure through the consumption of several food commodities. There are many factors involved in mycotoxin production by fungi but climate is the most important. Thus, when changes in the weather occur, mycotoxins production will be affected. We looked for articles that were available in scientific databases, written in English and that mention in the title and/or abstract the combined terms fungi and climate change and also mycotoxins and climate change. Nineteen articles were found: seven with the fungi and climate change terms and twelve with mycotoxins and climate change. Through the paper analyses, we noticed that some authors have stated that Portugal and others European countries with temperate climates have the biggest risk regarding exposure to fungi and mycotoxins. Additionally, a recently scientific report submitted to European Food Safety Authority stated that is expected a higher risk of contamination by Aflatoxin B1 related with the optimal conditions expected for *A. flavus* complex growth and proliferation in several food and feed products. Other fungi that can also increase its growth with global warming, specifically *A. ochraceus* complex that grow in high moisture environment and, consequently, we can expect also an increase of Ochratoxin A. The warm and humid weather also encourage crop infections caused by *Fusarium* sp., favoring, among this genus, *F. verticilloides* spread instead of *F. graminearum* and this can also lead to a change in the prevalent *Fusarium* mycotoxins in some crops. Although the increasing concern supported by several research groups that study the relation between climate changes and mycotoxins production, and also the possible impacts on public health, we still need new resources based on scientific data to support decisions and actions to prevent future fungi and mycotoxins contamination and exposure.

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### P03-066

#### Derivation of a threshold for genotoxic carcinogens: An insight into the procedure of the MAK Commission for compounds classified in Carcinogen Category 5



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The Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) proposes maximum workplace concentrations (MAK values) for volatile chemicals and dusts, biological tolerance values (BAT values), 'biologische Leitwerte' (BLW), biological reference values for workplace substances (BAR) and analytical methods for substances in the air and biological material. Substances which are carcinogenic, germ cell mutagenic, sensitising or absorbed percutaneously or which pose a risk during pregnancy are classified accordingly. The task of the MAK Commission is to provide comprehensive and authoritative information for health and safety professionals and researchers and to give scientific policy advice. Each year detailed documentation is published for all proposed MAK values, BAT values and classifications. Since January 2012 the MAK Collection has been available online in German and English. All publications that have appeared since 1972 are therefore available free of charge in electronic format: [www.dfg.de/en/mak](http://www.dfg.de/en/mak). To gain an insight into the procedure of the MAK Commission, this poster pro-

vides examples for the derivation of MAK values and allocation in the classification categories. Of particular interest are compounds classified in Carcinogen Category 5, substances that cause cancer in humans or animals or that are considered to be carcinogenic for humans and for which a MAK value can be derived. A genotoxic mode of action is of prime importance but is considered to contribute only very slightly to human cancer risk, provided the MAK and BAT values are observed. The reasoning behind the classification is illustrated by dichloromethane (MAK value 50 ppm) and isoprene (MAK value 3 ppm) with information on the mode of action, dose-dependence and toxicokinetic data.

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### P03-067

#### Development and validation of an analytical methodology for the determination of antipsychotic drugs in hospital wastewaters by gas chromatography–tandem mass spectrometry (GC–MS/MS)



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The consumption of psychiatric drugs has seen a huge increase during the last years as a consequence of the financial European crisis, and this can lead to psychological health effects causing several psychiatric diseases. These drugs have become pseudo-persistent in the environment due to their large volumes of use, and nowadays they are considered environmental emerging contaminants. Within this main group, the antipsychotic class have experienced an expressive increase in consumption, namely in Portugal, being used for the management of psychotic episodes as well as for other related behavioral symptoms and even other therapeutic indications. The present work describes the development and validation of a highly sensitive analytical method for the simultaneous determination of antipsychotic drugs in influent and effluent hospital wastewaters by GC–MS/MS. The studied compounds were levomepromazine, clozapine, chlorpromazine, haloperidol, quetiapine and ciamemazine using promazine as internal standard. Sample preparation was carried out by solid phase extraction (SPE) using mixed mode-columns (Strata XC – 200 mg) and followed by derivatization of the extracts with MSTFA (with TMCS). Chromatographic separation was achieved on a 5% phenylmethylsiloxane column. All chromatographic conditions and mass spectrometric parameters were previously optimized to enhance the maximum signal. The method was validated following internationally accepted criteria, and the studied parameters included selectivity, linearity, limits of detection (LOD) and quantification (LOQ), instrumental limits, precision and accuracy, stability and recovery. The procedure was linear for concentrations ranging from 0.1 to 10 µg/L (0.02–2 µg/L for haloperidol), with determination coefficients higher than 0.99 for all analytes. Intra- and inter-day precision was lower than 15% for all analytes at the studied concentrations, while accuracy remained between a ±15% interval. Recoveries ranged from 35% to 80%. Low LODs were achieved, between 2 and 10 pg/mL, allowing a reliable and accurate quantification of the analytes at trace level (low ppb). All studied parameters complied with the defined