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BOOK OF ABSTRACTS

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PESTICIDES

In Vivo Reactivating Efficacy of Oximes K203 and K027 Against a Direct Acetylcholinesterase Inhibitor: Dose-response Modeling

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Reactivation of organophosphate(OP)-inhibited acethylcholinesterase (AChE) as specific endpoint is used in efficacy testing of experimental oximes, antidotes in OPs poisoning. According to our best knowledge, the majority of *in vivo* studies tested only one or two oxime doses resulting in qualitative oxime efficacy evaluation. However, quantitative analysis of *in vivo* dose-response data would improve identification and quantification of the effect as well as rigorous comparison of different oximes efficacies. Thus, we have evaluated *in vivo* dose-response relationship for two promising experimental oximes, K203 and K027, concerning reactivation of AChE inhibited by dichlorvos (DDVP). To compare the oximes effects, benchmark (BMD) covariate approach was used to estimate oxime dose (with 90% confidence intervals) that elicits a pre-specified effect size of 100% (2-fold increase in AChE activity compared to DDVP-treated group). Wistar rats (5/group) were treated with oxime (1.25%, 2.5%, 5%, 25% and 50% LD_{50} *im*) immediately after DDVP challenge (75% LD_{50} *sc*). Activity of AChE was measured in erythrocytes by Ellman´s method 60 min after the treatment. Dose-response and BMD modeling was done in PROAST software (version 64.13, RIVM, Nederlands). Exponential model m5-b ($y=a[c-(c-1)\exp(-bx^d)]$) was selected as best estimate with parametes: a=0.8019, b_{K203}=0.0015, b_{K027}=0.003355, c=2.662 and d=1.218. Derived BMD_{100} were K203=194 (153, 243) and K027=100 (81, 125) μmol/kg bw, indicating that oxime K027 induces the same effect size with 2-times lower dose compared to oxime K203. Moreover, obtained confidence intervals of BMDs did not overlap allowing the conclusion that more potent dose-response relationship belongs to experimental oxime K027.

Keywords: benchmark dose, effect size, potency, erythrocytes, rat

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The Effect of Thiamine on Activity of Enzymes (with a special emphasis on MAPK) in the Brain of Japanese Quails Treated with Chlorpyrifos

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The aim of this study was to investigate the influence of vitamin B1 (thiamine) on biochemical changes in the brain tissue of Japanese quail (*Coturnix japanica*) treated with chlorpyrifos. The following parameters were examined: cholinesterase activity (acetylcholinesterase – AChE and butyrylcholinesterase – BChE), nitrite concentration–NO_2^- (parameter of oxidative/nitrosative stress), activity of inducible nitric oxide synthase –iNOS, arylesterase –ARE, cyclooxygenase –COX and extracellular signal–regulated kinase –ERK (MAPK).

The study was conducted on eighty male Japanese quails (2 controls and 6 experimental groups, n= 10), 3-4 weeks old. One control group was treated only with vitamin B1, while the second one received pure corn oil. CPF dissolved in corn oil was administered to three groups of quails by gavage for 7 consecutive days at doses of 1.5 mg/kg BW, 3 mg/kg BW and 6 mg/kg BW. Another three groups were treated with 10 mg/kg BW of vitamin B1 i.m. 30 min after CPF administration (in above mentioned doses) for 7 consecutive days. Our studies have shown that CPF

significantly inhibited both cholinesterases and ARE in brain, while vitamin B1 increased activity of enzymes in a dose dependent way. Also CPF has led to increase in the concentration of NO_2^-, activity of iNOS and COX, but after thiamine treatment there has been a decrease of these parameters. There has been a decrease of ERK expression after CPF treatment that demonstrates an increase of apoptotic vulnerability of cells exposed to CPF.

Overall these results confirm that CPF causes oxidative/nitrosative stress and apoptosis, but also support the hypothesis that thiamine belongs to the group of "antistress vitamins".

Keywords: acetylcholinesterase, butyrylcholinesterase, oxidative/nitrosative stress, arylesterase, apoptosis

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Evaluation of Biocidal Products Enquiries to the Austrian Poisons Information Centre 2015

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A biocidal product is any substance or mixture intending to destroy, deter, render harmless, prevent the action of, or exert a controlling effect on any harmful organism by any means other than mere physical or mechanical action. Biocidal products are divided into 4 main groups: disinfectants, preservatives, pest control and other biocidal products.

On behalf of and funded by the Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management the local Poison Information Centre (PIC) evaluated retrospectively enquiries regarding exposures to biocidal products in 2015.

PIC Austria received in total 25718 telephone enquiries in 2015. Regarding biocidal product exposure the PIC was contacted in 643 cases: 341 (53%) under the age of 15, 302 (47%) persons over 15 years of age. In 542 cases a poisoning could be excluded due to minor exposure. In 54 cases the risk of intoxication could not be estimated due to lack of sufficient information at the time of consultation. In 37 cases intoxication was suspected and medical observation was recommended. In only 10 patients an intoxication could be verified due to the severity of the symptoms. The causative substances were disinfectants (industrial n=5, household n=3) and chlorine gas (n=2).

In relation to the total number of calls, enquiries regarding biocidal products are relatively rare and the number of human intoxications seems to be small. Only 10 cases with severe symptoms, which had to be treated medically, were recorded. No deaths were recorded in the local PIC.

Keywords: biocide, consultation, intoxication

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Place of Oximes in the Management of Acute Poisoning with Cholinesterase Inhibitors: Experience of the Pharmacology Toxicology Department of University Hospital of Oran

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Acute poisoning with pesticides is a serious public health problem. The indication of oximes in the treatment of poisoning by anticholinesterase pesticides is still controversial in practice, although it seems theoretically interesting because of the reversibility of the toxic cholinesterase binding and the atropine-like effect. The aim of this work is to instigate, through our experience, a rational and scientific approach of the use of oximes in the treatment of acute anticholinesterase poisoning. This is a descriptive study of cases of acute pesticide poisoning received at Oran University Hospital during the last twelve years. Data was collected prospectively, using a pre-established information sheet, accompanying the samples. Diagnosis and monitoring were performed by the determination of cholinesterase activity. The interest of the oximes will be discussed through the analysis of some observations and a review of the literature. A total of 944 cases of acute pesticide poisoning were recorded, representing 10% of total acute intoxications. They occupy second place after drug poisoning. Among our patients, the indication of oximes, when available, has been justified in organophosphate poisoning, life-threatening carbamate poisoning, and in the presence of a severe cholinergic table where the pesticide is not identified but cholinesterase activity is collapsed.

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