



Preface

Bioanalysis of organophosphorus toxicants and corresponding antidotes

It is a great privilege that the *Journal of Chromatography B* devoted a special issue to the subject “Bioanalysis of organophosphorus toxicants and corresponding antidotes”. This special issue includes invited papers and selected papers from the *12th Medical Chemical Defence Conference* (MCDC, 22–23 April 2009, Munich, Germany). The MCDC is biannual international meeting of natural scientists and physicians from universities, international organizations, and governmental facilities all over the world dedicated to improve medical countermeasures, antidotes and therapies confronting the threat of chemical warfare agents and related poisons. Toxic organophosphorus compounds (OPCs) represent an important class of such toxicants.

OPCs are world-wide used as pesticides (sold and used as several hundreds of related chemical structures) and remaining stockpiles of nerve agents are still declared and present in military arsenals. According to the December 2009 annual report of the *Organisation for the Prohibition of Chemical Weapons* (OPCW) more than 28 metric tons of highly toxic organophosphorus nerve agents are still existent in controlled military arsenals and scheduled for contemporary destruction. Although banned by the international *Chemical Weapon Convention*, prohibiting development, production, stockpiling and use of chemical warfare agents, nerve agents still represent an important threat for military and civilian communities most likely by means of terrorist attacks and asymmetric warfare. Furthermore, intentional intake of OPC pesticides is a common and wide spread method for committing suicide not only in Asia causing more than 300,000 deaths per year.

After intake OPCs act as neurotoxins in mammals and insects causing inhibition of acetylcholinesterase by irreversible covalent binding thus evoking accumulation of the neurotransmitter acetylcholine in the synaptic cleft. Consequently, effector cells are permanently overstimulated leading to cholinergic crisis with paralysis of muscles and ultimately to death. If recognized early medical treatment of OPC poisoning after intoxication may be successful by administration of e.g. anticholinergic antidotes for symptomatic therapy (tropane alkaloids), enzyme reactivators (oximes) for causal therapy, and benzodiazepines as anticonvulsives in combination with supportive intensive care. The latter option unfortunately is of limited availability during terrorist attacks, thereby emphasizing the need for optimal antidotal effectiveness. Effective antidotal treatment of acute poisoning requires in depth understanding of interactions between the toxicant, compartments and biomolecules of the organism (toxicokinetics) as well as reliable data on therapeutics and their fate in the organism (pharmacokinetics).

Independent of the use in military conflicts or by terrorists, there is an actual and permanent entry of organophosphorus pesticides into the environment world-wide causing potential acute and chronic toxicity to man, environment and biota. Especially, pesticide residues in vegetables, fruits, grain, and water may provoke a cumulative risk to health. Therefore, several national and international programs for biomonitoring and risk assessment are initiated by e.g. the *US Environmental Protection Agency* (EPA) or the *European Commission*.

Sophisticated modern analytical tools for clinical and forensic samples are indispensable for evaluating the pathomechanism of action in vivo and in vitro as well as for biomonitoring and verification.

Therefore, this special issue presents instrumental analyses by qualitative and quantitative high-performance liquid chromatography, gas chromatography, high-performance thin layer chromatography as well as gel electrophoresis combined with on- and off-line electrospray and matrix-assisted laser desorption/ionization mass spectrometry or with biological functional assays. In addition, the meaningful enantio-selective properties of chiral OPCs and the current relevance of NMR techniques are referred and instrumental setups used in related pharmacological investigations of receptor binding and drug metabolism are considered.

This special issue outlines a unique compilation of research articles and reviews authored by researchers from leading organizations and institutions providing insight into state-of-the-art techniques currently used for biomonitoring and verification analysis of exposure to organophosphorus toxicants (pesticides and nerve agents) as well as for clinical monitoring of relevant therapeutics used to treat acute poisoning.

To conclude, we would like to thank all authors and reviewers for their valuable contributions and expert support allowing to realise this special issue. We are also thankful for the help provided by the journal's Editors, who gave us the possibility to focus on this field of bioanalytical approaches. In particular, we would like to thank Dimitros Tsikas who accompanied this project with great encouragement and effort during the initial proposal and later editorial phase.

We hope that this issue will be of interest for many researchers in the fields of separation science as well as of toxicological, forensic and clinical analysis.

Harald John studied chemistry at the Westfälische-Wilhelms University of Münster (Germany). In 1998 he finished his Ph.D. studies in the group of K. Cammann and W. Schlegel in Analytical Chemistry on the development and validation of immunological and chromatographic procedures for the determination of prostaglandins and related compounds in clinical samples. Following a period as a research associate at the Institute of Occupational Medicine, University of Münster, he moved to the

Lower Saxony Institute for Peptide Research, Hannover (Germany) for a postdoctoral fellowship. From 2000 to 2005 he has been Head of the Division of Analytical Peptide Chemistry at IPF Pharmaceuticals GmbH, Hannover, which was and is directed by W.G. Forssmann. The analytical division was responsible for the discovery, detection and structural identification of bioactive peptides from natural sources using combinations of immunological, chromatographic, capillary electrophoretic, and in particular mass spectrometric techniques. Based on this progress he has habilitated (postdoctoral university lecturing qualification) at the Humboldt-University of Berlin (Germany) in 2007 as an external scientist and pursues his *venia legendi* (Privatdozent, University Lecturer) in Analytical Chemistry at the same university. In the beginning of 2006 he changed to the Bundeswehr Institute of Pharmacology and Toxicology, Munich (Germany)—a national institution instructed to develop novel medical countermeasures and to improve therapeutic regimen for the treatment of poisoning with chemical warfare agents (CWA) and related toxicants. He has now focused on the development of analytical procedures applied to biological samples with toxicological, forensic or clinical relevance to determine highly toxic CWA and related organophosphorus pesticides as well as their relevant therapeutics and antidotes.

Horst Thiermann studied medicine at the University of Regensburg (Germany) and at the Technical University Munich (Germany) where he finished his doctoral thesis (MD) in 1988. From 1987 to 1989 he worked at the Bundeswehr Hospital Munich in the departments of anesthesiology and surgery and joined the Bundeswehr Institute of Pharmacology and Toxicology, Munich in 1989. Towards his qualifications as a Pharmacologist and Toxicologist (1996) and as a Clinical Pharmacologist (2002) he was working in research fellowships at the Walther-Straub-Institute of Pharma-

cology and Toxicology, Ludwig Maximilians-University Munich and at MDS Pharma Services, Höhenkirchen-Siegertsbrunn, Germany.

In 2005 he has habilitated (postdoctoral university lecturing qualification) at the Technical University of Munich as an external scientist and pursues his *venia legendi* (Privatdozent, University Lecturer) in Pharmacology and Toxicology at the same university.

Since 2006 he is heading the Bundeswehr Institute of Pharmacology and Toxicology. This institute is the German national competence centre on medical aspects against chemical warfare agents. The scientific focus is directed towards the improvement of medical countermeasures (e.g. therapeutic strategies) against poisoning by chemical warfare agents as well as the verification of exposure to such toxicants.

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