

Analytica Conference 2012 in München, Germany – Emerging Drugs of Abuse in Europe

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The Analytica Conference is a two-yearly, scientific event that complements the exhibition of the Analytica Trade Fair. This year, it took place in München (Germany) on April 17 – 20. It consisted of 24 sessions, with various topics on analytical, diagnostic, biochemical and molecular-biological methods and techniques. The Wednesday afternoon session was organized and directed by Prof. Dr. Dr. h.c. Hans H. Maurer, on behalf of the GTFCh (the German-speaking Society of Toxicological and Forensic Chemistry). It presented an overview of emerging drugs of in six interesting presentations. The presence of a large audience showed that the topic was highly valued.



Analytica Conference 2012 Speakers and Chairs: Michael Bovens, David M. Wood, Frank Mußhoff, Hans H. Maurer, Volker Auwärter, Melanie Müller, Michael Pütz.



The audience in the lecture hall.

Emerging Drugs of Abuse: What's on Today?

(Michael Bovens, Forensic Science Institute, Zürich, Switzerland)

Dr. Bovens presented us with an upgrade on the so called “Research Chemicals”, “Legal Highs” or “Designer Drugs”, which were seized by Swiss authorities in recent years. These substances belong to various chemical classes, such as amphetamines (e.g. fluoroamphetamine), cathinone derivatives (e.g. mephedrone, methylon, fluormethcathinone) piperazines (e.g. m-CPP, o-CPP), tryptamines, and more recently alkyl amines (e.g. geranamine), benzofuranes (e.g. 6-APB) and indanes (e.g. 5-IAI). Since the first seizure of synthetic cannabinoids (“Spice” in 2007) on the illegal drug market in Switzerland, the number of these substances has increased enormously. Their names generally have no chemical meaning, like JWH-, WIN-, CP-, HU-, AM- and URB- for cannabinoids. Dr. Bovens also gave examples of the professional appearance but sometimes poor quality of these products, like fraudulent ingredient listings despite holographic quality labels. He stressed that toxicological and pharmacological effects of these substances and their interactions are largely unknown. In Switzerland, changes to legislation have been made recently, in order to speed up and simplify the legal scheduling of these compounds.

From the Seized Sample to the Chemical Structure

(Michael Pütz, Federal Criminal Police, Forensic Science Institute, Wiesbaden, Germany)

Dr. Pütz discussed the instrumental-analytical challenges to forensic laboratories. The repertoire of designer drugs changes continuously and responds quickly to the scheduling of substances developed earlier. As a result, the analytical chemical characteristics of many of these compounds are only marginally known from the scientific literature and the compounds are generally not commercially available as reference standards. Methods that have proven to be helpful or even necessary for the elucidation of the chemical structures of completely new designer drugs are NMR and High-Resolution-MS. Analytical techniques that may rapidly analyze a sample are ion mobility spectrometry (IMS) and the combination of thin layer chromatography (TLC) and Desorption-Electrospray-Ionization-Mass Spectrometry (DESI-MS). Several examples were given. Many designer drugs have different positional isomers (e.g. RCS-4 and ortho-RCS-4 or the three chlorophenylpiperazines), different diastereomers (e.g. CP47,497-C8) or even different enantiomers (e.g. amphetamine and cathinone derivatives). Dr Pütz showed that stereoisomers might be investigated easily using capillary electrophoresis (CE) and CE-MS with chiral selectors, of which the analysis of dexmethamphetamine was a nice example.

Metabolism and detectability of emerging drugs of abuse

(Hans H. Maurer, Department of Experimental and Clinical Toxicology, Saarland University, Homburg (Saar), Germany)

Prof. Maurer stressed the importance of investigating the human metabolism of new drugs. This is important for the detection of the consumption, the abuse, and finally the risk assessment of new drugs. All these parameters can be estimated only if a suitable toxicological screening procedure exists to detect them or their metabolites in human biological samples. This holds true especially if only metabolites are excreted into the urine. The metabolizing enzymes and the kinetics of the drugs and metabolites should be known in order to assess further risks like drug-drug interactions and inter-individual variations, which may lead to increased side effects and poisoning. Prof. Maurer illustrated this by discussing the analysis and metabolic patterns of several new drugs of abuse such as 2,5-dimethoxy amphetamines, 2,5-dimethoxy phenethylamines, phencyclidine derivatives, beta-keto drugs (cathinones or pyrrolidinophenones), fentanyl derivatives and alkaloids of the herbal drug Kratom. The analysis of new drugs of abuse may be accomplished by liquid-liquid extraction, acetylation and GC-MS analysis (Maurer/Pfleger/Weber library, Wiley-VCH, Weinheim, 2011) or by LC-MSⁿ screening as described by Wissenbach et al. (Anal Bioanal Chem 2011, 400:3481).

Clinical signs and treatment of emerging drugs of abuse toxicity

(David M. Wood, Clinical Toxicology Service, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, UK)

Dr. Wood reported from his experience in general medicine, clinical toxicology and Poisons Information Services. He illustrated the use, the effects and the toxicity of new drugs such as mephedrone, mCPP and pipradol derivatives. He showed that clinical classifications (stimulant/depressant/hallucinogenic) do not always follow chemical classifications. Drugs with a similar chemical structure may have different pharmacological or toxicological profile. For instance, the ketamine analogue methoxetamine shows cerebellar toxicity, in contrast to ketamine which has prominent bladder toxicity. Dr. Wood also addressed poisonings with "Spice". They do occur and are accompanied by effects like agitation, tachycardia, high blood pressure and insults.

Current Knowledge of 3,4-methylenedioxymethamphetamine (MDMA) Neurotoxicity

(Melanie Mueller, Department of Neurology, The Johns Hopkins Bayview Medical Center, Baltimore, USA)

Dr. Melanie Mueller gave a thorough overview of the pharmacology and toxicology of MDMA, with special emphasis on the neurotoxicity. Neurotoxic effects may be evident from damage or anomalies of the cell body and nerve end. The exact mechanisms of neurotoxicity are yet unknown and differences between species exist. Proposed mechanisms of neurotoxicity include: a) neurotoxic metabolites of either the endogenous neurotransmitter or of MDMA itself; b) involvement of brain dopamine; c) glycogen depletion; and d) excitotoxicity. Levels of 5-hydroxyindoleacetic acid, the main metabolite of serotonin (5-HT), are reduced in the CSF of MDMA users and 5-HT transporters (SERT) are reduced in their brain. This will evoke neuropsychiatric sequelae such as cognitive deficits (e.g. impaired visual and verbal memory) correlating with the loss of SERT, alteration in circadian activity, changed sleep patterns, endocrine dysfunctions, impulsivity, and mood disorders, such as anxiety and depression. The clinical relevance of these neurotoxic effects was also discussed.

Spice, JWH & Co.: What's the current knowledge?

(Volker Auwärter, Institute of Forensic Medicine, University Medical Center Freiburg, Germany)

Dr. Auwärter focused on synthetic cannabinoids (aminoalkylindoles and others, "Spice"). Like Prof. Maurer, he stressed the importance of adequate (sensitive) bioanalytical methods and reference standards, not only for the compounds but also for their metabolites. A nice graph showed that the occurrence of new compounds in 'legal high' products was largely influenced by the scheduling of preceding substances. Clinical reports show that the effects and toxicity of synthetic cannabinoids are similar to those of cannabis in some aspects, but may be different in other aspects. "Spice" products (without concomitant use of other drugs) may show serious toxic effects such as generalized seizures, hypokalemia and nausea/vomiting (in combination with somnolence!). Psychosis and violence may also occur. Fatal cases have been reported, where the use of synthetic cannabinoids led to death indirectly. Recent toxicological tests suggest a carcinogenic (genotoxic) potential of some of the CB1 receptor agonists. All these (preliminary) data show that the toxicity of these compounds may be significantly higher than that of cannabis. This may become a serious threat to public health.