

## Letter to the Editor

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# New Psychoactive Substances: Risks and Challenges

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New psychoactive substances (NPS) have emerged in the last few years in response to market trends and legislative control. Only in the EU, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported in its European Drug Report 2016 the monitoring of more than 560 novel substances, of which 380 (70%) were detected in the past 5 years.<sup>1</sup>

NPS are usually drawn as analogues or derivatives of controlled substances, easy to obtain, inexpensive, not detected by standard toxicological screens and produced to circumvent regulations and imitate the effects of controlled drugs. Synthetic cannabinoids are among the most commonly seized NPS in Europe responsible for causing about 8 to 10 seizures per year, followed by cathinones. NPS are mainly manufactured in China and India, and purchased online via “darknets” (anonymous networks) without any age restriction. Other than phenethylamine, piperazine, tryptamine or aminoindan derivatives, compounds are also included in chemical classes of NPS.

The consumption or usage of a substance which “demands control”, is usually characterised by the following attributes: (a) the substance should be psychoactive (b) the usage or consumption of the substance should be associated with a motive of abuse or intoxication; and (c) the substance should possess certain characteristics which is capable of causing harm or threat to the human health. Traditional response to the discovery of a new ‘drug’ at a time when the discovery of such chemical compounds was a relatively rare event; necessitated the evaluation and assessment of the risks it poses to public health and accordingly include them in the national list of controlled substances. The current situation, marked by the discovery of many new substances and very limited evidence of related health risks, potentially stretches the credibility of the control systems.

Helander and Bäckberg<sup>2</sup> indicated that when launched, most NPS have not been tested on humans; increasing the risks of causing harmful and adverse conditions on the human health. Another potential threat to human health is due to the substances that are typically produced in the clandestine laboratories. The consequences of poor quality control in the production of these substances are attributed to unknown chemical structure, dose, and the presence of contaminants. Hence, dealing with medical complications associated with NPS use and overdose has become a growing problem at the emergency departments and intensive care units worldwide.

Previously, Baumann and Volkow<sup>3</sup> said that, although NPS can elicit subjective effects that resemble their progenitors, potential off-target sites of action are unknown and adverse medical consequences are common. Also, many of the case reports of intoxication are due to a combination of drugs and the lack of information concerning tolerance, routes of administration, dosage and sudden drug withdrawal syndrome meaning that reliable and accurate interpretation of NPS concentrations is not possible. A study published in the Australian Journal of Forensic Sciences in 2016 concerning the prevalence of new psychoactive substances in the Victorian fatally-injured drivers, reported that consumption of NPS can lead to a variety of psychological and physiological effects and these effects may last for a few to several hours

post dosage.<sup>4</sup> Repeated use of NPS can also lead to a more intense response and a longer duration of effect. The commonly reported responses towards synthetic cathinones include aggression, anxiety, euphoria, empathy, enhancement of mood and hallucinations. Synthetic cannabinoids have been shown to result in a dreamy state, confusion, depression, paranoia and psychosis. Different studies have indicated that, though the degree of impairment of driving skills caused due to NPS have not been reported, the impairment of cognitive and psychomotor functions due to NPS can affect motor skills required to keep a vehicle safe and on track on the roads, therefore possibly being considered as a public health risk.

In comparison to the classical controlled drugs, there are a lesser number of fatal cases reported and a limited amount of data available relevant in terms of examining the metabolism and toxicity caused due to NPS. However, there have been fatal cases of NPS reported continuously in USA, Europe, Japan and other countries.

The novel substances are typically not detectable with the usual drug of abuse immunoassays. It is therefore possible that they contribute towards acute toxicities and medical complications, or even deaths, by escaping detection. A major challenge is the lack of analytical research information available on these substances and the lack of reference standards since they are new to the market and consequently have not yet been characterized.

As reported by Lobo et al<sup>5</sup> sometimes the combination of different analytical techniques as nuclear magnetic resonance (NMR) spectroscopy, gas-chromatography–mass-spectrometry (GC-MS), fourier transform infrared spectroscopy (FTIR), high-resolution tandem mass-spectrometry (HR-MS/MS) and chemoinformatic tools, is necessary in order to confirm the true identity of these substances.

In relation to the interpretation of NPS concentration

in biological fluids, from a forensic point of view and according to Gerostamoulos et al<sup>6</sup> the major concern presently would be to establish minimum concentrations for the screening of NPS, to determine if the detection of the parent drug is adequate or whether metabolite screening is required. Overall, the qualitative detection of these drugs would enable the identification of NPS in casework much more readily than is possible under the existing situations, thereby improving the availability of prevalent related information. Unless the knowledge of the toxicity of these substances improves significantly using pharmacological studies, the toxicologists should be careful when determining the concentration of an NPS regardless of the matrix in which it is measured.

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