EDITORIAL

Current Design of New Psychoactive Substances

At the end of 2021, the European Monitoring Centre for Drugs and drug addiction as New Psychoactive Substances (NPS) was monitoring about 880 New Psychoactive Substances (NPS), 52 of which were first reported in Europe in 2021 [1]. These substances mimic the psychotropic effects of classical drugs of abuse but are not controlled by international drug laws, at least at the moment of their release in the illicit street and web market. Despite the apparent decrease in the number of compounds newly introduced to the European market starting from 2014-2015, the list of NPS released each year remains considerable [1]. Indeed, when an NPS is included in the banning laws of different countries, a new structural or functional analogue is introduced into the illegal dealing.

Differently from classic drugs of abuse, these new psychotropic moiety are scarcely studied from a physicochemical point of view and in their subjective and toxic effects [2, 3]. Information is based mainly on naïve news from users on the web fora. Conversely, since these substances represent an increasing alarm for the public health for the related fatalities and intoxication, investigating the newest compounds is extremely needed [4].

The objective of this Thematic Issue, divided into two parts, was to provide the most updated molecular and pharmacological knowledge of the upcoming NPS.

The issue opens with a review paper by Zaami and co-authors regarding the pharmacology and misuse insight of benzodiazepines (BDZs), designer BDZs and Z drugs [5]. These sedative-hypnotic compounds, prescribed for treating a broad range of conditions (e.g., anxiety, obsessive-compulsive disorders, phobias, sleep-related problems etc.), pose a serious public health problem since they are the most used prescribed drugs throughout the world. In recent years, there has been a large increase in the number of high potency designer benzodiazepines in the illicit markets where these substances may also appear as contaminants or be marketed in place of sedative and hypnotic NPS illicit drugs. Since their pharmacology and side effects have been scarcely investigated, this review paper fills a gap by providing all updated pharmacological studies and toxicity information on illicit benzodiazepines, including new designer benzodiazepines and Z drugs, whose increased consumption by vulnerable users can represent an ongoing health threat for teenagers or high-risk opioid drug users.

In order to disclose the trends in the pharmaceutical design of mostly dealt and consumed NPS in a selected area, a group of French investigators led by Jean Michel Gaulier, suggested analysing the oral fluid of drivers attending a music festival in South-West France [6]. Of the 265 individuals whose oral fluid was screened by liquid chromatography coupled with tandem mass spectrometry and high-resolution mass spectrometry, a 5% presented current consumption of 10 different NPS (APINACA, AB-Chminaca, 5F-AMB, 5F-PB-22, 2C-D, methoxetamine, ketamine, CMC, 4-MEC and euthylone) being the majority of the synthetic cannabinoids and synthetic cathinones. Comparing the obtaining results with those attained in 2017, an increase in the detection of these two latter classes of NPS was observed, reflecting consumption trends seen in more general populations in France.

Together with synthetic cannabinoids and synthetic cathinones, ketamine has recently increased its presence in the illicit NPS market after having been with GHB, the first NPS assessed by the European early warning system early at the beginning of the new century [7]. As reported by Varí et al., this anaesthetic drug moved from the medical world to that of recreational users since it was discovered that intense psychedelic experiences were obtained with dosages lower than those prescribed for anesthesia [8]. Its growing popularity was due to the fact that this NPS resulted cheaper than classical stimulants and that the amount used for recreational purposes does not cause respiratory depression. Notwithstanding the high number of acute intoxications and deaths related to exclusive ketamine use both in Europe and internationally, since 2015, there has been an increasing rise in the illicit ketamine market, and currently, the drug is being used with unprecedented peaks and a consequent significant increase in health risks for consumers.

The thematic issue closes with an interesting review on method development, validation and quality assurance for comprehensive screening approaches of drugs of abuse and NPS by liquid chromatography high-resolution mass spectrometry (HRMS) [9]. In 2017, this group of investigators already described in this journal standard practices for method development and validation in forensic toxicology [10, 11]. Conversely, up to date, few guidelines specifically addressed HRMS issues concerning compound identification, validation, measurement uncertainty and quality assurance. In the attempt to implement the use of this technique for targeted and untargeted screening of both classic drugs and NPS, 26 HRMS-based methods published between 2011 and 2021 were reviewed. In this regard, analytical data, such as sample matrices, analytical platforms, numbers of analytes and employed mass spectral reference databases/libraries., and the studied validation parameters were summarized and discussed. Data interpretation with a particular focus on identification criteria was also included together with current recommendations for the validation and determination of measurement uncertainty of qualitative methods.

We hope this thematic issue will be a valuable contribution for the readers interested in these updated studies and reviewers on the pharmaceutical design of NPS and its influence on the toxicity and consequent health threats for consumers.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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