Harnessing the power of mass spectrometry for early novel psychoactive substances (NPS) detection

SCIEX solutions for both targeted an non-targeted screening. Left: SCIEX Triple Quad™ 7500 LC-MS/MS System – QTRAP® Ready
Right: SCIEX X500R QTOF System.

The increased prevalence of novel psychoactive substances (NPS) in the recreational drug market has been a major contributor to the ongoing opioid crisis. NPS are newly emerging compounds designed to mimic existing recreational drugs that have emerged as potent alternatives to controlled opioids and frequently used as adulterants or cutting agents to commonly abused drugs. Continuous abuse of these substances can result in severe intoxication and, in some cases, fatal overdose.

Over the years, the surge of NPS and other synthetic drug classes has dramatically shifted the landscape of the drug market. What was previously characterized as a small subset of illicit drugs has now turned into a plethora of novel substances comprised of various chemistries — each inducing unique physiological effects. The dynamics of this growing interplay continues to pose serious safety concerns for public health and law enforcement officials alike that has resulted in a global public health crisis. The nature of this transformative shift has critical implications for the effective monitoring of these emerging substances. Since their potency and composition is highly variable, fast and comprehensive drug screening approaches are critically needed to enable accurate and timely identification of these emerging novel substances.

Traditionally, the detection of illicit substances has been performed using immunoassays or gas chromatography-mass spectrometry (GC-MS), however these techniques have their limitations. The use of immunoassays for designer drug screening is limited by the need to develop antibodies specific to an increasingly wide array of new chemical structures, proving a challenge for the dynamic and rapidly evolving nature of the NPS market. In addition, immunoassays are renowned for low specificity, cross-reactivity and are prone to a high rate of false negative results. Furthermore, immunoassays often need multiple panels to detect the wide range of NPS, because of the ever-expanding panels of pharmacologically active and toxicologically hazardous NPS. This disadvantages the speed at which the analytical process can be carried out. GC-MS, by contrast, requires lengthy sample preparation which slows the analytical process significantly. Overall, the similarity in molecular composition, transformative nature over time and the ever-expanding panel of pharmacologically active and toxicologically hazardous NPS makes their identification increasingly difficult for forensic toxicologists.

Liquid chromatography tandem mass spectrometric analysis (LS-MS/MS) is providing forensic toxicologists the speed and confidence required to reliably identify NPS and other novel synthetic drugs of abuse. Over the years, the gain in sensitivity compared to GC-MS, and the highly accurate analytical nature of tandem MS has become the preferred method for analysis of NPS over traditional techniques, for both screening and confirmation. Mass spectrometry enables characterization of NPS by assessing their mass, molecular weight and fragmentation pattern, providing the necessary information to elucidate their ever-evolving molecular structure. The data acquired by mass spectrometers provides analyte specific results which enables accurate quantification with far greater sensitivity and specificity than previously used techniques.

More recently, high-resolution mass spectrometry (HRMS) has emerged as a powerful and comprehensive tool for the characterization of NPS by reliably providing accurate mass, isotope pattern and MS/MS fragments that can be used to identify designer drugs using spectral library matching. These attributes have enabled toxicologists to specifically correlate mass measurements and molecular formulas to elucidate the molecular profile of an NPS. Where other nominal mass instruments rely heavily on fragmentation of these substances as a chemical fingerprint, HRMS provides an additional level of specificity by incorporating the chemical formula into criteria for positive identification. Likewise, acquisition of accurate mass MS/MS fragments is enabling toxicologists to reliably piece together the chemical structure of an NPS based on the accurate mass data acquired during HRMS experiments. The acquisition of full scan, high-resolution mass spectra in both MS and MS/MS modes also enables retrospective data analysis without the need to re-run the sample. This strategy is very attractive considering the ever-changing landscape of NPS in the drug market.

In recent years, the MS expertise developed by forensic toxicology laboratories for the early identification and detection of NPS has provided public health professionals and law enforcement agencies with a clearer picture of the emergence of NPS on the drug market.

This collective effort has proven to be an effective, team-based approach to staying ahead of the transformative NPS trends and continuously monitoring their evolution.

This critical information will strengthen existing responses to the emergence of NPS and provide the level of scientific intelligence to support NPS surveillance, monitoring, response efforts and drug policy formulation.

This eBook, brought to you by SCIEX, serves as a comprehensive resource for NPS-related content. In addition to general NPS information, it contains a repository of technical notes and webinars highlighting some of the recent scientific advancements developed by the forensics team at SCIEX and their collaborators. The portfolio of analytical instruments, workflows and integrated software solutions is presented as a comprehensive arsenal of tools available for forensic laboratories conducting NPS screening and identification. Also included in this eBook are testimonials from current passionate scientists describing how they leverage SCIEX technology in their laboratory and the challenges they face. Overall, this eBook has been designed to bring together all the necessary tools and resources to make the leap to LC-MS/MS for NPS screening and identification.

References

1. List of Announcements. (2020). Retrieved 26 June 2020, from **https://www.unodc.org/LSS/Announcement?type=NPS**

2. Hagan, A., & Smith, C. (2017). A New Beginning: An Overview of New Psychoactive Substances. Retrieved 26 June 2020, from **https://medcraveonline.com/FRCIJ/a-new-beginning-an-overview-of-new-psychoactive-substances.html**

3. Peacock, A., Bruno, R., Gisev, N., Degenhardt, L., Hall, W., & Sedefov, R. et al. (2019). New psychoactive substances: challenges for drug surveillance, control, and public health responses. The Lancet, 394(10209), 1668-1684. doi: 10.1016/s0140-6736(19)32231-7