Identifying 'designer' drugs taken by overdose patients

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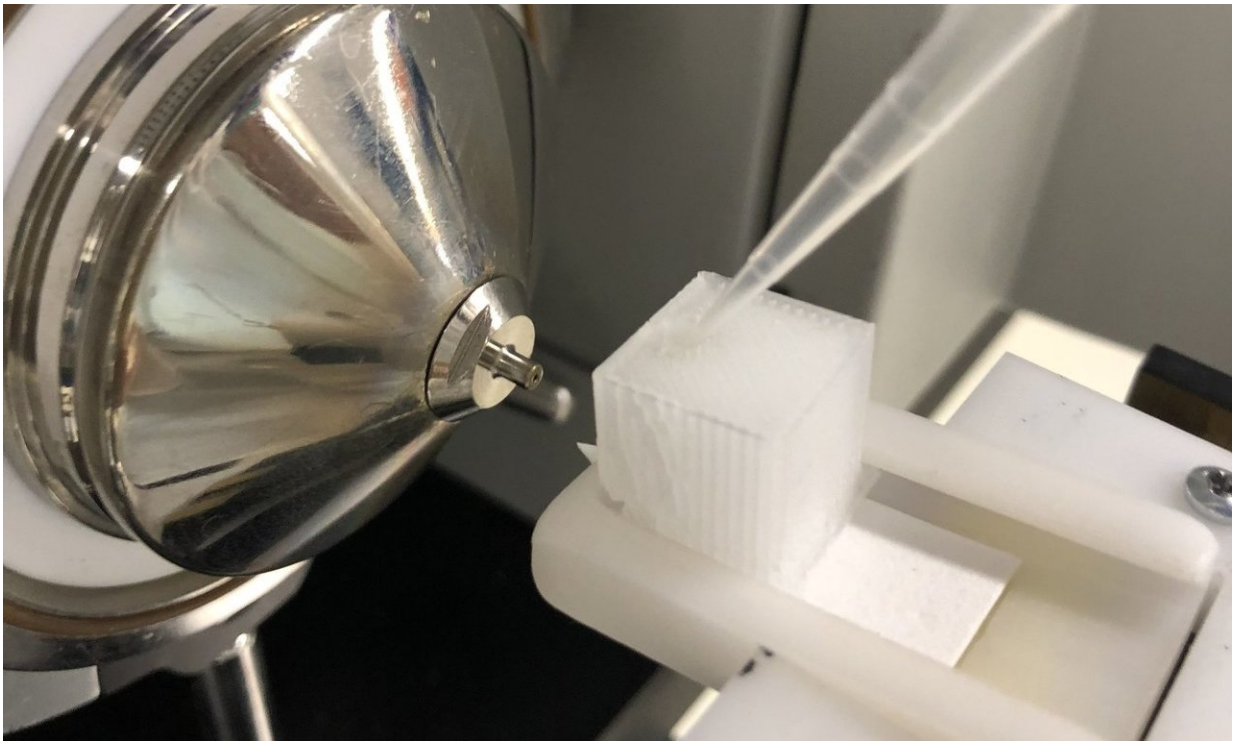

Drugs released from the test cartridge (center) are identified by a mass spectrometer (left). Credit: Greta Ren

Drug overdoses are taking a huge toll on public health, with potent synthetic drugs posing a particular threat. Medical professionals are scrambling to meet the growing demand for emergency room treatment, but they're hampered by the lack of a quick and easy test to screen

patients for these "designer" drugs. Chemists have now developed such a test and are refining it with the hope that hospitals could eventually use it to choose the appropriate treatment.

The researchers are presenting their results today at the 255th National Meeting & Exposition of the American Chemical Society (ACS).

"Hospitals can test for some drugs, like methamphetamine or cocaine, and those tests are pretty fast," Nicholas E. Manicke, Ph.D., says. "But for the new drugs, like fentanyl and synthetic cannabinoids, they would have to collect a blood sample and ship it to a toxicology lab. They wouldn't get the results back for weeks. In a life-or-death situation, that won't work, so they never do the test." Manicke hopes his developmental screening system could someday be used in emergency departments to identify the drugs responsible for a patient's overdose within one or two minutes.

The need is clearly growing. Overdose deaths from all opioids—which are responsible for two-thirds of drug overdose deaths—more than doubled from 2006 to 2016, according to the U.S. Centers for Disease Control and Prevention. More specifically, the impact of synthetic opioids such as the prescription painkillers fentanyl and tramadol is even more devastating, with deaths increasing six-fold over that same period.

The new test could help medical staff counter these trends. Early in the project, Manicke approached Daniel E. Rusyniak, M.D., a professor of emergency medicine at Indiana University, for his insights on screening for illicit drugs. Based on his experience, Rusyniak advised Manicke to focus on emerging synthetic drugs because there wasn't a good way to screen for them in the clinic. Manicke and his team at Indiana University-Purdue University Indianapolis went on to build a device that can screen for these compounds, as well as for classic illicit drugs.

The key component is a small, inexpensive and relatively simple disposable cartridge that contains a solid-phase extraction medium. When a small amount of plasma is placed on the cartridge, the medium pulls any drugs out of the plasma and concentrates them. The drugs are removed from the extraction medium by a drop of solvent, and then they are ionized to produce an array of molecular fragments. Each type of drug produces a different assortment of fragments that serve as a distinctive chemical signature for that particular compound. A mass spectrometer detects the fragments. Software is then used to identify the specific drugs that were in the blood sample from the readout. The whole process takes less than five minutes. Graduate student Greta Ren says the technique is flexible because the database used to identify drugs can be expanded to include new ones, as needed.

With the device, Ren is analyzing blood samples from Indianapolis emergency room patients who appeared to have overdosed on drugs. At the ACS meeting, the team is announcing their first results on those clinical samples. The test successfully identified drugs in the samples, including fentanyl and its synthetic analogs, synthetic cannabinoids, and traditional drugs such as methamphetamine and lorazepam. That's a major achievement because some of these drugs are so potent that users only take a tiny amount, so the drug concentration in blood is very low. In some cases, the test couldn't distinguish between drugs with very similar molecular structures. To improve those distinctions, the researchers are adjusting the way they analyze data from the mass spectrometer.

Manicke says that initially, the device could be used to guide public health and public policy decisions, by shedding light on the types of drugs that are causing overdoses across Indiana. Down the road, he hopes it will be applied in emergency departments to guide the treatment of individual patients.

More information: Title: Detection of designer drugs from plasma via paper spray mass spectrometry

Abstract

Designer drug use has become more widespread over the last few years, and there is a need for a fast, simple, and sensitive drug screen. Most designer drugs are very potent and are typically found at the sub-ng/mL to low ng/mL concentrations in users' blood. In order to achieve the desired sensitivity while also maintaining a simple analytical method, a disposable paper spray cartridge with an integrated solid phase extraction (SPE) column was utilized.

Plasma spiked with drugs and deuterated internal standards was analyzed on a previously reported SPE cartridge. The plasma sample was loaded at the top of the SPE column and allowed to wick through to an absorbent waste pad. After drying, the sample holder was moved to the top of the paper substrate (Whatman 31ET paper cut into a triangle). A spray solvent (acetonitrile with 0.1% formic acid) was applied at the top of the SPE column and a 4kV voltage was applied over 2 minutes. Paper spray analysis was performed on a Thermo TSQ Vantage operated in the MRM mode as well as a Thermo Q-Exactive Focus.

A paper spray ionization method with integrated SPE cartridge was developed and optimized for detection of two synthetic cannabinoids: JWH-200 and JWH-250. Extraction solvent compositions, solid phase material, amount of solid phase material, sample volume and wash step were investigated. Solvent composition and increased sample volume had the most significant improvement in performance.

Limits of detection in plasma for synthetic cannabinoids ranged from 0.1-0.5 ng/mL and for fentanyl and its analogs ranged from 0.1-0.3 ng/mL. In order to show the potential for quantitative analysis, calibration curves (0.1 ng/mL - 50 ng/mL) with isotopically labeled internal standards were attained and had good linearity ($R2 > 0.96$). The method was used to analyze authentic samples, which were collected from two Emergency Departments in Indianapolis from suspected

overdose patients. Fentanyl, several fentanyl analogues, synthetic cannabinoids and traditional drugs were successfully detected and quantified.

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