

Review article



Updates in Chemical Analysis of Drugs of Abuse

Ghadeer M. M. Abdelaal*

Department of Forensic Medicine & Clinical Toxicology, Faculty of Medicine, Zagazig University, Egypt

ABSTRACT

***Corresponding author:**Ghadeer Mohamed
Mahmoud Abdelaal**E-mail:**

ghadeer.mma@gmail.com

ORCID:

0000-0001-8598-1028

Introduction: Drug abuse is a worldwide crisis, and illicit drug testing is widely applied daily both clinically and forensically. Gas chromatography-mass spectrometry (GC-MS) is the traditional confirmatory gold standard for drug testing and is used for non-targeted substance screening, however, it is limited to volatile non-polar compounds. Liquid chromatography-tandem MS (LC-tandem-MS) has become a new gold standard for its ability to identify more types of analytes (polar and non-polar). In contrast to GC-MS, it is not suited for non-targeted drug screening as different optimal parameters are set for each drug. **Aim:** Describe the advanced techniques for testing illicit substances and then, recommend the most appropriate ones for point of care (POC) settings. **Results:** High-resolution-MS (HRMS) such as time of flight MS (Tof-MS), made the analysis of compounds of same molecular masses but with different formulas possible. Quadrupole Tof-MS is suited for non-targeted substance screening. Another novel technology is the emergence of miniature ambient ionization MS, that is portable and can analyze unprepared samples in native environment within one minute. Ion mobility spectrometer (IMS) is another advance that can identify compounds including isomers with high resolution within seconds and portable devices are available. Portable Raman and near infrared (NIR) spectrometers have allowed fast screening for drugs and have been efficiently used for other on-site forensic applications. Hence, these advanced techniques are promising for quick detection of illicit drugs in a POC setting. **Conclusion:** HRMS is an accurate comprehensive method for qualitative and quantitative testing in laboratory settings. Miniature ambient ionization MS is very rapid with no sample preparation, but it is more expensive than other alternatives in POC testing. Thus, the best methods for POC drug testing are portable IMS, portable Raman spectrometer, and handheld NIR spectrometer for their accurate, easy, and quick analysis within seconds with affordable costs.

Keywords: High resolution MS, Time of flight MS, Miniature ambient ionization MS, Ion mobility spectrometer, Raman spectrometer, Near infrared spectrometer.

INTRODUCTION

Abuse of drugs has become a worldwide crisis; its detrimental effects are not limited to the health hazards of the abusers but also it causes massive social and economic costs (Xue et al., 2020). Moreover, the use of some of these drugs has been legalized in some countries and laws have been established for this purpose. For instance, the law of driving under the effect of drug in the United States that requires highly effective on-site quantitative testing in biological specimens (Kang et al., 2020).

There is an overlap between illicit drug testing between forensic toxicology applications and clinical toxicology settings. Forensic toxicology tests drugs in the context of human performance (e.g., impaired driving, workplace testing and sports doping) and death (postmortem toxicology) in a wide range of sample matrices. In contrast, clinical toxicology deals with the impact of these substances in both acute toxicity and long-term monitoring and specimens are mainly urine and blood (Borden et al., 2020).

A great challenge in illicit drug analysis is the continuous appearance of new psychoactive substances (NPS). Thus, analysis via routine methods is no longer helpful in screening of NPS due to the lack of the structural information of these substances which is needed for targeted analysis. Researchers are developing non-targeted techniques to overcome this obstacle (Fu et al., 2019).

To detect illicit substances, a preliminary test, such as an immunoassay or a color test, is used to determine the possible

presence of the substance. If the preliminary test is positive, the rest of the seized sample is forwarded to the laboratory for confirmation. Typically, the laboratory will repeat the preliminary test and then use a confirmatory technique (Hoffmann and Jackson, 2015).

Among drug of abuse testing procedures, mass spectrometry (MS) is the most discriminate. It is the current gold standard in illicit drug analysis, measuring the precise molecular mass of ions by their mass to charge ratio (m/z). Separation, ionization, and detection are all required in MS. Gas chromatography and liquid chromatography can be used for separation (Harper et al., 2017).

The traditional gold standard for confirmatory drug analysis is gas chromatography- MS (GC-MS). To produce gas-phase ions, electron impact was the first ionization technique used. This method is a type of hard ionization, where ionization results in breaking of the chemical bonds of the molecule generating fragment ions. The ability of GC-MS to perform a non-targeted comprehensive drug analysis is due to the presence of a comprehensive and universal electron ionization mass spectra library. However, it is limited to thermo-stable and volatile compounds with low molecular weights (Maher et al., 2015).

Liquid chromatography- MS (LC-MS) is considered a new gold standard. The most common LC-MS used in clinical laboratories is LC-tandem-MS, as it allows multiple stages of MS to be performed. It is equipped with two mass analyzers in tandem and a collision cell in the middle. LC-tandem-MS can monitor ion transitions from precursor ions to product ions, which improves its capability to detect and quantitate the analytes. Usually, the mass

analyzers are quadrupoles which are considered of low-resolution as they detect a molecular mass with a precision of 1 atomic mass unit (amu). They are commonly used in targeted drug analysis as each substance has a different optimal parameter (Tamama, 2020).

The time needed to receive an analytical response is at the heart of the concerns in testing illicit drugs. The average run time for a GC or LC is 20 to 30 minutes, not including sample preparation time, which generates workloads on forensic laboratories (Hoffmann and Jackson, 2015). The drawbacks of these confirmatory techniques are the need for extensive sample preparation, the long time required for separation, and the destructive nature of the process. Moreover, these methods use relatively large instruments which makes them not suited for fast analysis at point of care (POC) and street levels (Coppey et al., 2020).

Therefore, the development of techniques for non-targeted, rapid, sensitive, and on-site detection of illicit drugs is essential. Thus, researchers have been working on developing quick and portable devices for drugs of abuse analysis.

The aim of this review is to describe the most updated techniques for testing drugs of abuse and then, recommend the most appropriate ones for POC settings.

METHODS

Several procedures were followed to ensure a high-quality review of the literature on updates of illicit drug testing.

First, a comprehensive search of peer-reviewed journals, but not conference papers, was completed based on a wide

range of key terms including drug testing, HRMS, Tof MS, ambient MS, miniature MS, portable IMS, portable Raman spectroscopy and portable NIR spectroscopy. Five databases were searched including: Elsevier, Google Scholar, PubMed, Springer, and Wiley Online Library. Second, the reference section for each article found was searched in order to find additional articles. Third, key forensic toxicology and analytical journals from around the world were searched independently and included the following: Analyst, Analytica chimica acta, Analytical chemistry, Annual review of analytical chemistry, Applied spectroscopy, Bioanalysis, Clinica chimica acta, Clinical biochemist reviews, Drug testing and analysis, Egyptian journal of forensic sciences, Engineering in agriculture, environment and food, Forensic science international, Frontiers in chemistry, Harm reduction journal, Mass spectrometry reviews, Reviews of modern physics and science.

The search process uncovered 21 peer-reviewed articles published from 2004 to 2021 and a book published in 2019 titled 'Bioinformatics and Drug Discovery'.

RESULTS

This review covers high-resolution MS, miniature ambient ionization MS, ion mobility spectrometry, portable Raman spectroscopy, and handheld near infrared spectroscopy as examples of the most updated techniques for detection of drugs of abuse.

I. High-Resolution Mass Spectrometry (HRMS)

High-resolution MS has drawn great interest among forensic toxicologists to advance the non-targeted comprehensive testing of illicit drugs, including NPS in both

forensic toxicology and clinical analysis (Fu et al., 2019).

It can detect a molecular mass with an accuracy of 0.001amu, thus it can discriminate compounds of same molecular masses but with different chemical formulas. The principle of Time-of-flight MS (ToF-MS), which represent HRMS, implies that all ions enter the ToF in pulses; so, the duty cycle is relatively high. LC-HRMS is commonly available as hybrid MS as LC-quadrupole ToF-MS (Q-ToF-MS), in which ToF mass analyzer is attached to a quadrupole mass analyzer in front and a collision cell in the middle. Data about both precursor and product ions can be provided in high resolution (Tamama, 2020).

The first quadrupole (Q1) can operate as a mass filter for specific ion selection based on their m/z ratio, or in radio frequency (RF) only mode where all ions are transmitted. The second quadrupole (Q2) is a collision cell where ions are bombarded by neutral gas molecules e.g., nitrogen, causing fragmentation of the ions. Also, the Q2 can operate in RF-only mode without fragmentation of ions. Then, ions are reaccelerated into the ToF analyzer where they are pulsed by an electric field and accelerated orthogonally to their primary direction. All ions have gained the same kinetic energy and enter the flight tube, a field free drift region, where mass separation takes place. Ions with a lighter mass will have a shorter time of flight, while heavier ions will take longer time through the flight path to the detector. Q-ToF-MS application to comprehensive drug screening offers great advantages in the rapidly changing drug landscape (Allen and McWhinney, 2019).

II. Miniature Ambient Ionization Mass Spectrometry

A great advance in MS was made by the emergence of electrospray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI). These ionization techniques are soft (i.e., ionizes the analyte with little or no fragmentation, thus the abundance of the molecular ion is increased). ESI and MALDI widened the molecular-weight range of MS to megadalton (MDa), thus made ionization of large molecular-weight biomolecules possible. Recently, molecular ionization techniques have progressed to the point of recording mass spectra on specimens in their native environment which ambient ionization MS (Maher et al., 2015).

Miniature ambient ionization MS has developed as a breakthrough in mass-based technologies, in which specimens in the native state are directly sampled without any preparation, ionized in the ambient conditions, and then introduced into MS. Hence, it is promising in fast drugs of abuse detection in POC settings. It can be used to analyze liquid specimens after being spotted on paper, screen luggage for explosive materials, and detect illicit drug in fingerprints (Tamama, 2020).

II.1. Ambient Ionization Mass Spectrometry:

Ambient ionization develops ions outside MS from samples in their indigenous state without any prior preparation. In 2004, the desorption electrospray ionization (DESI) was reported as the first ambient ionization technique (Takats et al., 2004). Since then, more than forty methods of ambient ionization have been described (Kerian et al., 2014).

II.1.1. Desorption Electrospray Ionization (DESI):

Desorption electrospray ionization (DESI) is an ESI-related technique where direct desorption/ionization takes place. In DESI, charged solvent particles impact the surface of the specimen under native conditions resulting in extraction and ionization of the analytes and propelling them into the inlet of the MS for analysis. This technique can be applied to solid phase analytes. Analysis of a liquid specimen can be done if spotted and dried on a solid material. DESI-MS is widely used for surface analysis. It is used to analyze dried blood and urine spots, in addition to the fast detection of illicit drugs on fingerprints (Figure 1) (Cooks et al., 2006).

Despite the ability of DESI to examine large molecules up to 66,000 Da, this wide range is usually unnecessary in forensic practice where tiny compounds predominate. DESI has been used in many forensic applications such as detection of

illegal drugs, explosives, and ambient imaging and examination of latent fingerprints (Hoffmann and Jackson, 2015).

Ifa et al., (2008), has demonstrated the forensic application of DESI imaging in latent fingerprints analysis (Figure 2).

By recording data at multiple points within a latent fingerprint, DESI-MS imaging (DESI-MSI) can produce an image based on any specific ion (e.g., illicit substance, explosives, agrochemicals, etc.) that is present in sufficient amounts to be identified. Also, endogenous substances present on skin (e.g., fatty acids and lipids) can be detected and identified. This chemical signature not only provides information about the identity of the person, but also reveals details about his recent activities, diet, and medications. Latent chemical prints have been imaged from different surfaces (e.g., glass, plastic, and paper). Moreover, overlapped prints can be distinguished from each other (Wu et al., 2013).

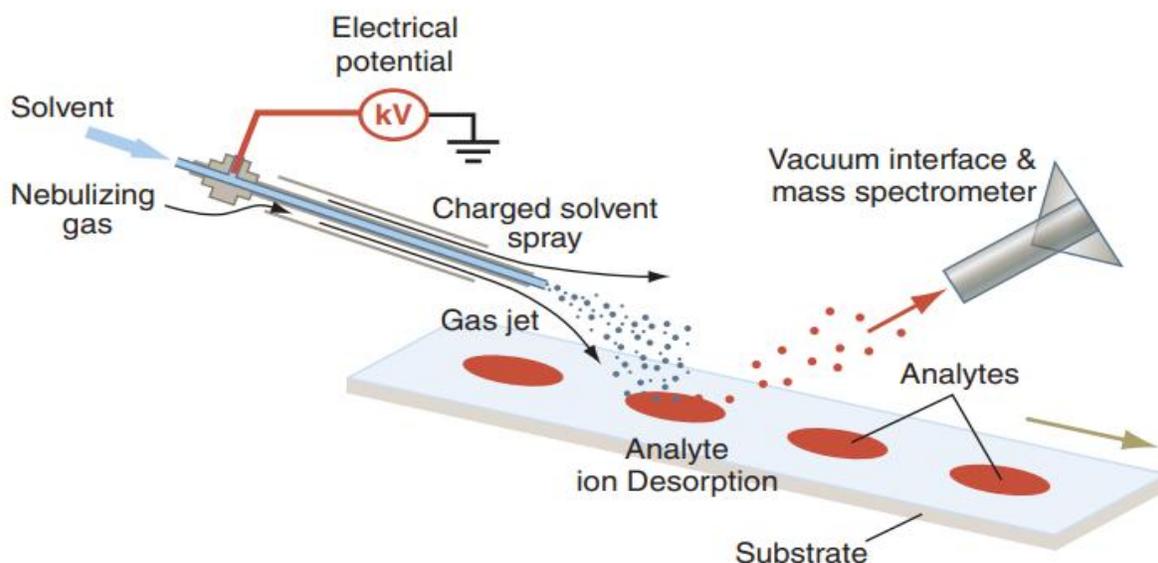


Figure 1: Desorption electrospray ionization for ambient analysis of samples without preparation. Reprinted with permission from (Cooks et al., 2006).



Figure 2: (a) DESI image showing cocaine distribution on a latent fingerprint. (b) Computer-developed fingerprint from DESI image, and the red dots are points of minutiae that are automatically detected. Reprinted with permission from (Ifa et al., 2008).

II.1.2. Direct Analysis in Real Time (DART):

Direct analysis in real time (DART) is a two-step ambient ionization technique. First, thermal desorption of the analyte from a liquid or solid specimen (sampling step). Thus, the analyzed compounds should be thermally stable and volatile. Then, the analyte reacts with charged solvent particles or metastable atoms (reaction step). The metastable nitrogen or helium gas reacts with ambient molecules (e.g., oxygen or water) to produce reactive ions, which ionize the thermally desorbed analytes before being injected into the MS. (Figure 3) (Tamama, 2020).

In contrast to DESI, DART is confined to compounds with a molecular weight less than 800 Da. It has been applied for different forensic applications such as detection of illegal drugs, chemical warfare agents, explosives, and ignitable liquids (Hoffmann and Jackson, 2015).

Direct analysis in real time allows fast non-destructive analysis and can quantify when combined with an internal standard. Furthermore, a pill can be held in front of the gas stream to determine the molecular species present in seconds (Harper et al., 2017).

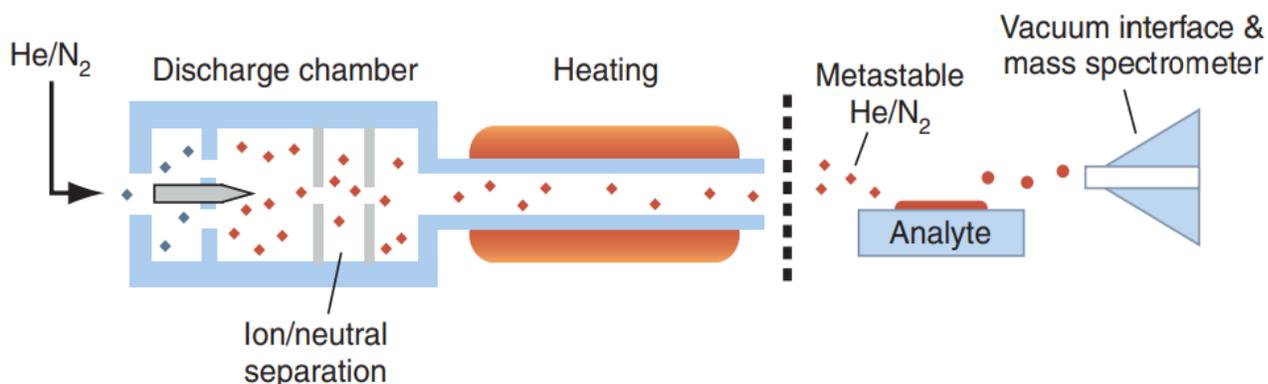


Figure 3: Direct analysis in real time for ambient analysis of samples without preparation. Reprinted with permission from (Cooks et al., 2006).

II.2. Miniature Mass Spectrometry:

Portable MS is another significant advance for MS application at POC. In the last decade, several miniature MS devices have been revealed for coupling ambient ionization with direct analysis of substances such as backpack miniature MS (Kang et al., 2020).

Although miniature ambient ionization MS is a promising update for on-site fast drug detection, it has several technical limitations. Ambient ionization is subjected to changes of ambient conditions (e.g., humidity, temperature, and air pollutants) as well as low reproducibility due to specimen properties that affect desorption and entrance of the analyte ions into the MS. It also skips the chromatographic separation; Thus, samples with complex matrices are prone to strong matrix effects and isomeric compounds are difficult to be discriminated (Kuo et al., 2019 and Tamama, 2020).

III. Ion Mobility Spectrometry (IMS)

Although MS techniques are selective and can assign a molecular formula for a target analyte based only on its molecular mass, isomeric species are difficult to be differentiated by them, even with tandem-MS. Ion mobility spectrometer (IMS) is able to structurally characterize isomers (compounds with the same chemical formula but different atomic arrangements). Despite being traditionally used to study large biomolecules (e.g., proteins), it has been recently applied to smaller molecules (<400 Daltons) such as drugs (Phillips et al., 2019).

In IMS, the sample is introduced into the ionization chamber via a carrier gas to create ions. An electrical grid transports these

ions to the drift tube (the heart of the IMS). An electric field and a drift gas separate ions based on their varied mobility in this tube. Small ions travel faster than larger ions, therefore they get at the detector first. The ions detected using a Faraday plate which develops a current. For generation of a mobility spectrum, this current is amplified (Kafle et al., 2016).

Ions are separated based on how fast they move through the carrier gas. Ion mobility is determined by three molecular properties: the charge, mass, and the collision cross section of the ion. IMS can detect one part per billion (ppb) (i.e., one molecule in a billion) and is highly selective. Internal standards or prebuilt procedures can be used for quantification. Analysis takes a few seconds even for a complex specimen. Fast and accurate testing, ease of use, low cost and minimal maintenance make it one of the best techniques of drug analysis. Some gas analyzers are able to update online, allowing for quick sharing of methodologies and novel molecular species among clinics instantly (Harper et al., 2017).

Recently, handheld IMS has been developed to be used as a field portable system in airports for detection of illicit drugs and explosives, and in combat areas to detect chemical weapons (Kafle et al., 2016).

A drawback of drift tube IMS is its limited resolution for a fixed length drift tube, and because resolution is proportional to device length for a given weak electric field, making devices longer than few meters is impractical. Recently, ultra-high resolution IMS instruments was built by Structures for Lossless Ion Manipulations (SLIM) using travelling waves (Metz et al., 2017).

IV. Updates in Raman Spectroscopy

Raman spectroscopy is a scattering method that probes the molecular vibrations based on Raman Effect. The inelastic scattering of incident radiation (monochromatic light e.g., laser beam) is caused by its interaction with the vibrating sample molecules. Most of this scattered light has a frequency equal to that of the incident radiation (Rayleigh scattering). Only a small part of scattered radiation has a frequency different from that of the incident radiation (Raman scattering). In Raman spectrum, stoke lines appear when the frequency of incident radiation is higher than that of the scattered radiation. But if the frequency of incident radiation is lower than that of the scattered radiation, anti-Stokes lines appear (Bumrah and Sharma, 2016).

The recent technological updates in Raman spectrometers have widened their use in forensic practice. It generates a molecular-specific spectrum without any sample preparation. Also, it enables a non-destructive and a non-contact in situ analysis of powders, tablets, and liquids. This is of great importance regarding prevention of specimen contamination, and preservation of evidential material. Moreover, portable Raman systems have been successfully used as screening techniques in detection of drugs of abuse in drinks residue e.g., flunitrazepam (a date-rape drug) (Ali and Edwards, 2017).

The use of short wavelength lasers in Raman spectrophotometers enabled the use of remote fiber optic probes which can be applied over long distances (>10 meters). These fiber optic probes can record the Raman spectra in locations away from the sample site, thus prevent the exposure of

investigator to hazardous materials (Bumrah and Sharma, 2016). A man-portable Raman system assembled in a backpack containing spectrometer, detector, power supply and computer was used to detect unknown materials from distances up to 10 meters. This portable system weighed 14 kilograms and was used to identify heroin and cocaine (Hopkins et al., 2016).

Raman spectroscopy is a reliable and non-destructive technique for both qualitative and quantitative testing of various drugs of abuse and illicit substances of forensic interest. It analyzes solid and liquid samples very quickly and without removing them from their packaging, thus maintains the integrity of the forensic evidence. The simplification of spectra produced by resonance permits easy identification of species contained in complex mixtures. Weak Raman signals and strong fluorescence caused by impurities or colored packaging may result in low sensitivity. However, this difficulty was managed by combing two updates of resonance Raman and surface enhanced Raman spectroscopy (Bumrah and Sharma, 2016).

V. Updates in Infrared Spectroscopy

Infrared (IR) spectroscopy is a very discriminatory technique based on the measurement of specimens as a function of wavelength. By passing IR through a specimen and measuring the amount of incident radiation that is absorbed at each IR frequency, a spectrum is obtained. Interpretation of this spectrum enables identification of the molecular functional groups. The IR spectra of a pure substance produce a distinctive fingerprint that

differentiate it from IR absorption pattern of other compounds, including isomers. Virtually, all compounds possess IR active vibrational modes and can be tested both qualitatively and quantitatively. Although quantification of unknown can be done, it is difficult and need expert. Recent updates in IR technology have allowed portable IR devices (Harper et al., 2017).

Near-infrared (NIR) technology has been used for identification and quantification of illegal drugs and analysis of falsified pharmaceuticals. Portable analytical NIR devices e.g., handheld NIR are used for on-situ analysis of drugs and provides real-time data about the nature and the purity of the substance investigated. Thus, brings the laboratory to the field and aids the trend of

decentralization. On-site NIR device coupled with a cell phone application provides a rapid and reliable information about a questioned sample, hence avoiding systematic testing by the forensic laboratory. This technique is non-destructive to the samples, takes only a few seconds and provides both qualitative and quantitative data, in addition to geolocation information. Therefore, portable NIR spectroscopy coupled with a mobile application is a promising approach for on-site illicit drug analysis. However, unknown compounds such as NPS and substances in trace amounts are unlikely to be recognized by NIR spectroscopy (Coppey et al., 2020).

Based on this review, advantages and disadvantages of each updated technique are summarized in Table (1).

Table (1): Advantages and disadvantages of drug abuse testing updated techniques.

Updated Technique	Advantages	Disadvantages
High Resolution MS (Fu et al., 2019).	<ul style="list-style-type: none"> - Higher resolution than traditional MS. - Non-targeted comprehensive drug screening. - Can distinguish isomers. - Qualitative and Quantitative. 	<ul style="list-style-type: none"> - Large and expensive equipment (Not suited for POC testing). - Needs sample preparation (Destroy the sample). - Long analytical time.
Miniature Ambient Ionization MS (Kuo et al., 2019 and Tamama, 2020).	<ul style="list-style-type: none"> - Qualitative and Quantitative. - Use unprepared samples (Non-destructive). - Portable devices available (Suites POC testing). - Easy and rapid. (Takes seconds to minutes). 	<ul style="list-style-type: none"> - Changes in environmental conditions. - Low reproducibility. - Strong matrix effect. - Hard to differentiate isomers.

<p>Ion Mobility Spectrometry (Harper et al., 2017 and Metz et al., 2017).</p>	<ul style="list-style-type: none"> - Can distinguish isomers. - Qualitative and Quantitative. - Use unprepared samples (Non-destructive). - Portable devices available (Suites POC testing). - Easy and rapid (Few seconds). - Minimal maintenance. - Minimal cost for consumables. 	<ul style="list-style-type: none"> - Drift tube has a limited resolution for a given fixed length.
<p>Raman Spectroscopy (Bumrah and Sharma, 2016).</p>	<ul style="list-style-type: none"> - Qualitative and Quantitative. - Use unprepared samples (non-destructive). - Can analyze samples inside their packages. - Portable devices available (Suites POC testing). - Easy and rapid (Seconds to minutes). - Affordable costs. 	<ul style="list-style-type: none"> - low sensitivity due to weak Raman signals and strong fluorescence by impurities or colored packaging.
<p>Near-Infrared Spectroscopy (Coppey et al., 2020).</p>	<ul style="list-style-type: none"> - Qualitative and Quantitative with geolocation information. - Use unprepared samples (non-destructive). - Portable devices available (Suites POC testing). - Easy and rapid (Seconds to minutes). - Affordable costs. 	<ul style="list-style-type: none"> - Unable to recognize illicit drugs in trace amounts. - Unable to recognize NPS

MS: Mass Spectrometry

POC: Point of Care

NPS: New Psychoactive Substances

CONCLUSION

Chemical analysis of drugs of abuse is a daily process in both forensic and clinical practices. The illicit drugs and addictive substances lead to huge health, social and economic costs. Given the current drugs of abuse crisis worldwide and the emergence of NPS that can be missed by the traditional drug testing techniques, the need to update these analytical techniques has become of great interest.

The prime examples of updates in illicit drug analytical techniques are HRMS, miniature ambient ionization MS. HRMS has been used as a powerful technique for non-targeted comprehensive screening of illicit drugs, including NPS. It can identify compounds of similar molecular weights but with different formulas. Miniature ambient ionization MS, on the other hand, is still in the investigational phase to overcome many technical obstacles before being widely applied in forensic and clinical testing.

Ion mobility spectrometer is easy, fast, sensitive, selective, and non-destructive technique that requires minimal maintenance and cheap consumables. Quantification is possible without expert technician, and online updating is available. It can distinguish molecules having same formula, but different atom arrangement (Isomers). Thus, IMS is the ideal choice for clinics with a moderate funding. Portable IMS is currently available and is used in airports for detection of narcotics.

The best updates for POC drug testing are portable Raman and handheld NIR spectrometers. They are superior in almost every way to other techniques from a cost-benefit view. These technologies are

small, simple to use and allows effective identification of unknown analytes. However, they are still rather expensive, and quantitation requires advanced expertise. These devices are currently used by in law-drug enforcement settings.

In summary, advanced portable/handheld devices for rapid, sensitive, and on-site identification of illicit substances have become available. These technical updates in drug testing could contribute to the decentralization trend of the laboratory confirmatory techniques to POC settings.

RECOMMENDATIONS

1. Miniature MS needs further research to overcome its limitations regarding sampling and matrix effect of complex specimens.
2. Portable analytical devices of IMS, Raman and NIR techniques are currently available, however, a wider partnership between health care agencies and companies who produce them is needed to discuss their possible utility in POC settings by more affordable costs.

REFERENCES

- Ali, E. M. and Edwards, H. G. (2017): The detection of flunitrazepam in beverages using portable Raman spectroscopy. *Drug testing and analysis*. 9: 256-259.
- Allen, D. R. and Mcwhinney, B. C. (2019): Quadrupole time-of-flight mass spectrometry: A paradigm shift in toxicology screening applications. *The Clinical Biochemist Reviews*. 40: 135.
- Borden, S. A., Palaty, J., Termopoli, V., Famiglini, G., Cappiello, A., Gill, C. G. and Palma, P. (2020): Mass spectrometry analysis of drugs of abuse: challenges and emerging strategies. *Mass spectrometry reviews*. 39: 703-744.

- Bumrah, G. S. and Sharma, R. M. (2016): Raman spectroscopy–Basic principle, instrumentation and selected applications for the characterization of drugs of abuse. *Egyptian Journal of Forensic Sciences*. 6: 209-215.
- Cooks, R. G., Ouyang, Z., Takats, Z. and Wiseman, J. M. (2006): Ambient mass spectrometry. *Science*. 311: 1566-1570.
- Coppey, F., Becue, A., Sacre, P.-Y., Ziemons, E. M., Hubert, P. and Esseiva, P. (2020): Providing illicit drugs results in five seconds using ultra-portable NIR technology: An opportunity for forensic laboratories to cope with the trend toward the decentralization of forensic capabilities. *Forensic science international*. 317: 110498.
- Fu, S., Stove, C. and Elliott, S. (2019): Advances in analytical methods for drugs of abuse testing. *Frontiers in chemistry*. 7: 589.
- Harper, L., Powell, J. and Pijl, E. M. (2017): An overview of forensic drug testing methods and their suitability for harm reduction point-of-care services. *Harm reduction journal*. 14: 1-13.
- Hoffmann, W. D. and Jackson, G. P. (2015): Forensic Mass Spectrometry. *Annual Review of Analytical Chemistry*. 8: 419-40.
- Hopkins, A. J., Cooper, J. L., Profeta, L. T. and Ford, A. R. (2016): Portable deep-ultraviolet (DUV) Raman for standoff detection. *Applied spectroscopy*. 70: 861-873.
- Ifa, D. R., Manicke, N. E., Dill, A. L. and Cooks, R. G. (2008): Latent fingerprint chemical imaging by mass spectrometry. *Science*. 321: 805-805.
- Kafle, G. K., Khot, L. R., Sankaran, S., Bahlol, H. Y., Tufariello, J. A. and Hill JR, H. H. (2016): State of ion mobility spectrometry and applications in agriculture: A review. *Engineering in agriculture, environment and food*. 9: 346-357.
- Kang, M., Zhang, W., Dong, L., Ren, X., Zhu, Y., Wang, Z., Liang, L., Xue, J., Zhang, Y. and Zhang, W. (2020): On-site testing of multiple drugs of abuse in urine by a miniature dual-LIT mass spectrometer. *Analytica chimica acta*. 1101: 74-80.
- Kerian, K. S., Jarmusch, A. K. and Cooks, R. G. (2014): Touch spray mass spectrometry for in situ analysis of complex samples. *Analyst*. 139: 2714-2720.
- Kuo, T.-H., Dutkiewicz, E. P., Pei, J. and Hsu, C.-C. (2019): Ambient ionization mass spectrometry today and tomorrow: Embracing challenges and opportunities. *Analytical chemistry*. 92: 2353-2363.
- Maher, S., Jjunju, F. P. and Taylor, S. (2015): Colloquium: 100 years of mass spectrometry: Perspectives and future trends. *Reviews of Modern Physics*. 87: 113.
- Metz, T. O., baker, E. S., schymanski, E. L., renslow, R. S., thomas, D. G., causon, T. J., webb, I. K., hann, S., smith, R. D. and teegarden, J. G. (2017): Integrating ion mobility spectrometry into mass spectrometry-based exposome measurements: what can it add and how far can it go? *Bioanalysis*. 9: 81-98.
- Phillips, S. T., Dodds, J. N., May, J. C. and Mclean, J. A. (2019): Isomeric and Conformational Analysis of Small Drug and Drug-Like Molecules by Ion Mobility-Mass Spectrometry (IM-MS). *Bioinformatics and Drug Discovery*. Springer.
- Takats, Z., Wiseman, J. M., Gologan, B. and Cooks, R. G. (2004): Mass spectrometry sampling under ambient conditions with desorption electrospray ionization. *Science*. 306: 471-473.
- Tamama, K. (2021): Advances in drugs of

abuse testing. *Clinica Chimica Acta*. 514: 40-47.

Wu, C., Dill, A. L., Eberlin, L. S., Cooks, R. G. and Ifa, D. R. (2013): Mass spectrometry imaging under ambient conditions. *Mass spectrometry reviews*. 32: 218-243.

Xue, W., Tan, X., Oo, M. K. K., Kulkarni, G., Ilgen, M. A. and Fan, X. (2020): Rapid and sensitive detection of drugs of abuse in sweat by multiplexed capillary based immunobiosensors. *Analyst*. 145: 1346-1354.

الجديد في التحليل الكيميائي للعقاقير المخدرة

غدير محمد محمود عبدالعال*

قسم الطب الشرعي و السموم الإكلينيكية، كلية الطب البشري، جامعة الزقازيق، مصر

مقدمة: يمثل تعاطي المخدرات أزمة عالمية كبيرة، كما أن تحاليل الكشف عن المخدرات تتم يوميا على نطاق واسع في الطب الإكلينيكي والشرعي. ويعد المعيار الذهبي التأكيدى لاختبارات العقاقير هو جهاز كروماتوغرافيا الغاز- مطياف الكتلة (GC-MS) ، و لكن أصبح جهاز كروماتوغرافيا السائل- الترادف- مطياف الكتلة (LC-tandem-MS) معياراً ذهبياً جديداً لقدرته على تحديد مركبات أكثر تنوعاً. ولكنه، على عكس GC-MS ، غير مناسب لفحص الأدوية الشامل الغير محدد.

الهدف من البحث: وصف التقنيات الحديثة فى تحاليل المواد المخدرة ، ومن ثم التوصية بأدسب هذه التقنيات للتطبيق المباشر فى نقاط الرعاية (POC).

طرق البحث: تم البحث فى خمس قواعد بيانات علمية بناء على الكلمات المفتاحية للبحث.

النتائج: جعل جهاز مطياف الكتلة على الدقة (HRMS) مثل مطياف الكتلة بوقت الرحلة (ToF-MS) تحليل المركبات ذات الكتل الجزيئية المتماثلة ولكن بصيغ كيميائية مختلفة ممكناً ، و ذلك لقدرته التفريقية (Resolution) العالية. ويعتبر مطياف الكتلة الرباعي - بوقت الرحلة Quadrupole ToF-MS مناسباً لتحليل المواد الشامل غير المحدد. كما يعد ظهور الأجهزة المصغرة من مطياف الكتلة ذات التأين فى الوسط المحيطي تقنية جديدة أخرى ولكنها محمولة ويمكنها تحليل العينات فى بيئتها دون تحضير فى غضون دقيقة واحدة. بالإضافة إلى، مطياف الحركة الأيونية (IMS) والذى يعد تقدم آخر يمكنه تحديد المركبات المختلفة بما فى ذلك الأيزومرات بدقة عالية فى غضون ثوانٍ و يوجد منه أجهزة محمولة. و أخيراً سمح مطياف رامان (Raman) و مطياف الأشعة تحت الحمراء القريبة المحمولان (NIR) بإجراء فحص سريع للأدوية فى أماكن تواجدها واستخدامها بكفاءة فى تطبيقات الطب الشرعي الأخرى. وبالتالي ، فإن هذه التقنيات المتقدمة واعدة للكشف السريع عن العقاقير غير المشروعة فى نقاط الرعاية (POC).

الخلاصة: بناءً على هذا البحث ، يعد جهاز مطياف الكتلة على الدقة (HRMS) تقنية شاملة و دقيقة للتحاليل النوعية والكمية للمواد المخدرة ولكن كبر حجم أجهزته جعلته مناسب فقط للإستخدام فى المعامل. بينما، تعد الأجهزة المصغرة من مطياف الكتلة ذات التأين فى الوسط المحيطي مناسبة للإستخدام المباشر فى نقاط الرعاية لكونها سريعة جداً و بدون الحاجة إلى تحضير للعينات، ولكنها أعلى من البدائل الأخرى . وبالتالي ، فإن أفضل الطرق للكشف عن المخدرات فى نقاط الرعاية هي الأجهزة المحمولة من مطياف الحركة الأيونية (IMS) ، ومطياف رامان (Raman) ، ومطياف الأشعة تحت الحمراء القريبة (NIR) و ذلك لقدرتها على الكشف الدقيق بسهولة عن المخدرات فى غضون ثوانٍ ، بالإضافة إلى تكاليفها المعقولة.

التوصيات: فى ضوء نتائج هذه الدراسة نوصي بالآتى:

1. عمل دراسات أخرى للبحث عن حلول لمعوقات أجهزة مطياف الكتلة ذات التأين فى الوسط المحيطي فيما يتعلق بأخذ العينات وتأثير المصفوفة (Matrix effect) على جودة النتائج فى العينات المركبة.
2. توسيع الشراكة بين منظمات الرعاية الصحية والشركات المنتجة لأجهزة التحليل الكيميائي المحمولة لتقنيات IMS و Raman و NIR المتاحة حالياً، لمناقشة فائدتها فى الكشف عن المواد المخدرة فى نقاط الرعاية POC و توفيرها بتكاليف معقولة.