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MINIATURIZED AND PORTABLE DEVICES FOR ON-SITE DRUG ANALYSIS

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ABSTRACT

Historically, drug analysis has been the domain of centralized laboratories with access to sophisticated instrumentation such as HPLC, GC-MS, and LC-MS. Although these "gold standard" approaches possess extremely high sensitivity and absolute accuracy, they are limited by high expense, slow turnaround times, and a need for specialized operators—characteristics that make them unsuitable for rapid, on-site analysis. However, recent breakthroughs in miniaturization, microfluidics, portable spectroscopy (such as Raman and NIR), and electrochemical sensing technologies have driven a paradigm shift towards decentralized analysis. These advances have made possible the creation of compact, intuitive "point-of-need" devices for rapid, real-time analysis in forensic, clinical, and environmental contexts. By leveraging the power of smart materials and smartphone interfaces, these devices represent a revolutionary approach to drug analysis. This review article offers a thorough examination of the history of development of these technologies, grouping the various analytical platforms now in use. We assess their particular applications, balancing the substantial benefits of portability and rapid analysis with the present limitations of these platforms in terms of detection limits and regulatory issues. Finally, we consider future directions, focusing on the possibility of autonomous, high-throughput on-site analysis to revolutionize global drug monitoring and public health safety.

KEYWORDS: Portable analytical devices. Point-of-need testing. Microfluidics. On-site drug analysis. Miniaturized spectroscopy. Electrochemical sensors.

INTRODUCTION

Miniaturization has emerged as a prominent trend in the field of analytical chemistry, making it possible to miniaturize laboratory methods without compromising their analytical performance. This trend is revolutionizing modern analytical instruments, particularly in applications where fast, precise, and economical chemical analysis is needed. Some of the developments in this area include the miniaturization of gas chromatography (GC), liquid chromatography (LC), microbore columns, and capillary and microfluidic systems.[1] These systems enhance the sensitivity of the analysis while reducing the operating costs. These characteristics are especially important in situations where only small or valuable samples are available, such as biological or clinical samples, and in unusual environments such as those encountered during space missions. Miniaturized analytical systems often offer higher separation efficiency compared with conventional analytical instruments. The improved mass transfer and reduced band broadening result in sharper chromatographic peaks and better resolution. When these systems are coupled with highly sensitive detection techniques such as mass spectrometry (MS), their performance is further improved. The low flow rates employed in miniaturized systems enhance ionization efficiency and enable lower detection limits, making them ideal for trace component identification in complex samples. Analytics tools in a mini-sized format are primarily created to allow analysis of small sample sizes; while these can be low in numbers (but can yield high-informative value) and often too low in volume to allow for reliable application of more conventional large analytical process(es). Conventional analytical processes generally require a large sample volume, and consume lengthy periods of preparation time as compared to the time required with use of mini-sized analysis.[2]

Miniaturizations of conventional analytical processes allow for reliable assessment of small sample sizes with very little or no sample preparation time; thus, enabling reliable assessment of very small sample sizes with minimal or no sample preparation prior to actually performing the analysis. Furthermore, use of miniaturization of analytical systems provides both economic and environmental benefits. Small-sized systems require substantially less solvent and materials to perform analyses; thus, significantly reducing the cost of the operation, and reducing the environmental impact of the operation. An example, where miniaturization of conventional liquid chromatography (LC) methods is in compliance with the principles of Green Chemistry, Green Analytical Chemistry, and Green Sample Preparation is as follows: Portable and miniaturized LC instrumentation can be used to analyze samples directly at the location where the samples were collected, thus eliminating any degradation of the sample during transport, and any chance for cross-contamination or residual waste that occurs due to the sample being transferred to another location.[3,4] An extreme example of this trend is nano-liquid chromatography (nano-LC), which can reduce solvent consumption by up to a thousand times when compared to conventional LC systems. Micro-scale columns, compact detection units, lab-on-a-chip devices, and the use of 3D printing technologies to create portable and integrated analytical platforms are examples of recent advancements in this field. These developments have greatly improved the functionality and performance of miniaturized LC systems over the last ten years. The advantages, technological advancements, and unresolved issues related to miniaturized liquid chromatography are highlighted in this review of recent developments.[5]

EVOLUTION OF PORTABLE DRUG ANALYSIS

Early methods

Immunoassays and basic colorimetric test kits were the mainstays of the first portable drug analysis techniques.

Colorimetric kits are simple to use in field settings like forensic investigations or law enforcement operations because they produce a visible color change when a particular drug or chemical group is present. Compared to straightforward color tests, immunoassays, which use antibodies that bind to target drug molecules specifically, increased the selectivity of detection. These early methods did, however, have significant drawbacks. Their cross-reactivity frequently decreased specificity, resulting in false positives or incorrect identification, and their sensitivity was comparatively low, making it challenging to detect trace amounts of drugs. For accurate results, confirmatory laboratory-based methods were still necessary.[6,7]

Advances in miniaturization

We have made progress in shrinking the size of drug detection tools. With analytical technology advancing, miniaturization completely changed drug detection systems. The development of fluid devices made it possible to do complex chemical tests in very small spaces using only a little sample and reagent. Miniaturization helped a lot here. At the time improvements in tiny materials like nanoparticles, carbon nanotubes and sensors with special structures made detection more sensitive and selective. These tiny materials are really good at detecting things. These advancements resulted in the creation of lab-on-a-chip platforms. Lab-on-a-chip platforms can do steps like sample prep, separation and detection all on one small device. This is really handy for drug detection. Additionally handheld spectrometers based on techniques like Raman, infrared or fluorescence spectroscopy were developed. These handheld spectrometers can quickly identify drugs in the field without damaging them. They are really useful, for detecting drugs on the go. Miniaturization made all this possible.[8,9]

Digital integration

More recently, the integration of digital technology has further improved the potential of drug analysis systems.

Smartphones have become a powerful tool for gathering, processing, and communicating information. The integration of a smartphone with a portable sensor or optical device allows users to collect analytical information, automatically process the information with the help of a specific smartphone application, and store or transmit the results instantaneously with the help of a cloud-based system. The integration of AI technology allows users to rapidly interpret complex analytical information, increasing the accuracy of results with minimal human intervention.[10,11]

LC BASED ON CHIP

The miniaturization of analytical instrumental configurations and the development of micro total analysis systems (μTAS) is driven by the need for reduced samples, reagents, and increased speed of analysis. All these factors are highly required by the principles of GC and GAC. In this context, devices such as lab-on-chip (LOC) have been designed for the miniaturization of analytical procedures with reduced solvents.[12] The integration of analytical and micro-electromechanical systems (MEMS) has resulted in the development of microfluidics, which has enabled the miniaturization of chromatographic instrumental configurations. LC-chips, which refer to microfluidic liquid chromatography chips, provide a number of advantages such as reduced samples and reagents, faster analysis, and the potential for miniaturization. However, LC-chips have a number of disadvantages related to the founding principles of chromatography, which include reproducibility, packing, and compatibility.[13]

These disadvantages associated with LC-chips can be eliminated using the various technologies for constructing microfluidic systems, especially because the advantages that can be obtained from the instrumental configurations are

significant: i) reduced samples and reagents; ii) faster analysis; iii) miniaturization/integration with other microfluidic systems to develop automated analytical systems; iv) high potential for high throughput; v) cost-effectiveness.[14]

In addition, in certain instances, the LC chips can be configured to be disposable, thus preventing any form of cross-contamination or carryover in the system. Moreover, the system meets the basic GC guidelines, which are as follows:

- Minimal amount of samples/reagents used
- Eco-friendly solvents used
- Reduced amount of waste generated
- Biodegradable/biocompatible materials used

LOC devices have five advantages over traditional systems, as outlined in:[15]

- Precision: Accurate control of microflows
- Speed: Faster analysis, which is critical in screening tests
- Cost: Reduced costs, as in the case of the materials used as well as the operation cost
- Volume: Efficient operation with minimal samples required
- Complexity: Requires expertise to operate.

Table 1: Miniaturized Chromatographic Columns[15]

Column Type	Internal Diameter	Stationary Phase	Key Advantage
Microbore LC	1–2 mm	Packed silica	Reduced solvent use
Capillary LC	0.1–1 mm	Packed particles	High sensitivity
Nano-LC	<0.1 mm	C18 stationary phase	Extremely low flow rates
Monolithic column	Variable	Porous monolith	Low backpressure

The concept of LOC allows for the full integration of analytical procedures, such as preparation, separation, and detection, on a microchip, thus allowing for the possibility of automation and parallelization.[16] In this scenario, the possibility of the use of automated multi-LC-chip devices also allows for their use in space missions. Mass spectrometry is the most commonly used detection technology, owing to its high selectivity and sensitivity.[17] Chip-based LC-MS is a powerful technology for proteomics, especially for the identification and quantification of peptides from complex biological samples, owing to the limited number of samples in proteomics.[18] LOC technology also has the possibility of being used in the rapid detection of pathogens in foods and water, especially in a combination with Microfluidics and Polymerase Chain Reaction technology.[19,20] Currently, the integration of LOC technology with MS detection technology is allowing for breakthroughs in low-volume, high-throughput screening with continuous online monitoring and sample preparation, thus necessitating the need for robust data and standardized protocols reproducibility and accuracy.

Gritti and co-workers reported that an optimal LC system in microchips should be able to perform under pressures up to 10,000 bar and should be compatible in terms of integrated sample injection and detection, as well as chromatographic mobile phases.[21] However, LC systems in microchips are not yet able to fulfill all these criteria, especially regarding the high pressures.

The main properties of materials used in the fabrication of LC-chips: mechanical strength, transparency in the UV/Vis region, absence of nonspecific adsorption, biological compatibility, and gas permeability. It is obvious that polymers are preferable because they are not only less expensive and suitable for mass production but also allow the adjustment

of their properties by chemical modification. A wide variety of polymeric materials have been used to fabricate microchips, but certainly the most popular one is polydimethylsiloxane (PDMS).[22] Another one is polyimide, which is compatible with most organic solvents and in a wide pH range. Of particular interest are ceramic and titanium-based materials, which have been attracting the interest of researchers because of their mechanical strength, thermal, and solvent stability.[23]

In liquid chromatography, miniaturization usually implies the use of columns with internal diameters less than 1 mm.

These columns include capillary LC columns and nano-LC columns. The small column diameter implies that the injection volumes and mobile phase flow rates employed during the analysis are much lower than those used in traditional LC techniques. The first parameter to be optimized during miniaturization is the particle size of the stationary phase.[24] The use of small particle size provides a much larger surface area, which increases the resolution of the chromatogram. However, it has been observed that a small particle size increases the backpressure of the system.

This increased backpressure may not be sustainable by the instrument, leading to a lack of reproducibility of the analysis. To improve this limitation, researchers have been working on developing novel materials for the stationary phase. The novel materials should provide a high degree of separation while at the same time minimizing backpressure.[25] Although packed columns dominate the field of LC, other columns such as open tubular columns and monolithic columns have been considered due to their flexibility and lower backpressure. The most commonly used stationary phases are reversed-phase materials, especially C18 phases. Most researchers synthesize their own materials to reduce the costs.[26]

Another issue with miniaturized systems is developing reproducible ways to pack tiny particles. One way to resolve this is to make the stationary phases in situ, or by using microfabricated structures that simulate packed particles.

Monolithic phases have significant potential since their highly porous structure minimizes backpressure and can be created in situ inside microchannels via photopolymerization. Other advantages include the ability to customize both the morphology and chemical functionality of the monoliths for specific applications and the ability to integrate multiple monoliths with distinct properties on a single chip. The progress in LC-chip technology has led to an increased interest in fabrication techniques, especially with regard to the use of additive manufacturing (3D printing). This technique offers flexibility, low cost, and fast development of analytical devices. Although miniaturized columns provide many benefits (e.g., higher sensitivities, quicker analyses, less solvent consumption), they require careful method development and handling. Integration of microfluidic chips represents another significant technological development.[27] In this new technology, it is possible to have precise control of fluid flow at the micro-scale, and combine sample preparation, separation and detection all in one platform. By doing this, both dead volume and efficiency are improved. However, challenges still exist in manufacturing of the chips. Specifically the mechanical strength and compatibility between materials can be problematic as many chip materials cannot handle very high pressure.[28]

In the miniaturized LC (liquid chromatography) systems, the stationary phase is instrumental in separating analytes based upon their chemical or physical interactions (e.g., through adsorption). Figure 1 shows portable LC. The most commonly used materials for the stationary phase include porous solids (i.e., silica, alumina, polymers), thin films, gels

and monolithic structures. The most frequently used fabrication processes to combine these stationary phases into a microfluidic device are photolithography, etching, and thin-film deposition. Usually, particles less than 2 μm are employed to produce greater plate numbers (i.e., a smaller amount of band broadening) and sharper peaks during chromatographic analysis. In addition, a narrow particle size distribution must be maintained since this reduces band broadening and increases separation efficiency.[29]

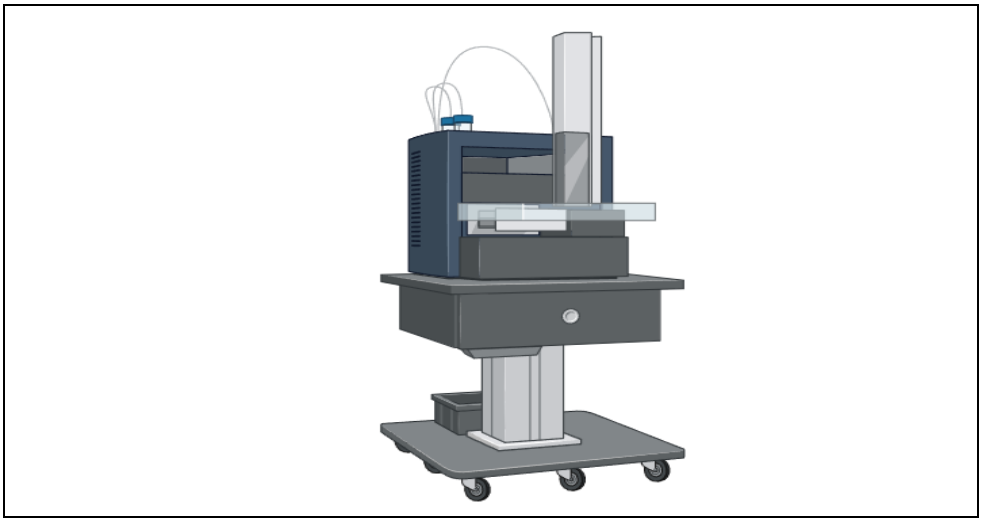

Figure 1: Portable LC.

COLORIMETRIC ANALYSIS

The outcomes of qualitative chemical color tests are restricted by the subjective nature of visual assessments made by the analyst. This issue is further complicated by the varying lighting conditions under which color tests are conducted; for instance, a test carried out under fluorescent light in a lab may yield different results than one performed outside on a cloudy day. Efforts to enhance result objectivity have introduced colorimetric, spectrophotometric, and digital image analysis methods to chemical color testing. Although the use of portable colorimeters and spectrophotometers for field analysis of color spot test results is constrained, there is increasing research in the realm of digital image analysis due to its ease of use. Choodum et al. first established the possibility of digital image analysis for semiquantitative analysis by applying it to the results of basic presumptive color tests for amphetamine, methamphetamine, and opiates.[30] A digital camera was utilized in these early investigations to gather the digital image in regulated illumination, and the Red, Green, and Blue (RGB) color values were obtained using image processing software after the image was sent to a computer. Calibration curves are created by taking use of the correlation between the illicit drug concentration and the intensity of RGB values.[31] A quicker, portable, more convenient, and real-time method of digital picture analysis was made possible by developments in mobile phone technology and functionality. A portable smartphone's built-in camera and open-source apps, like ColorAssist, are used to take a digital picture of the color test and extract the RGB components all at once.[32] The quantitative analysis of methamphetamine has effectively used this method of digital image processing. employing sol-gel sensors and presumptive color tests. The intrinsic limits of these presumptive tests still exist, even though digital image analysis has increased the usefulness of a straightforward chemical color test for illegal drugs.[33] By converting RGB coordinates into histograms and using the chemometric methods of simple linear correlation for univariate analysis and principal components analysis (PCA) for multivariate exploratory analysis, certain smartphone apps (like PhotoMetrix) further improve the system's portability and convenience.[34] A sample

holder, an illumination source, an image capture device, and a computer for color histogram extraction and chemometric model creation are the four fundamental parts of an analytical colorimetric system. It is impossible to quantitatively analyze changes in the concentration of colored chemical species with the unaided eye, but research has proven that digital image-based analysis can accomplish this.[35]

VIBRATIONAL SPECTROSCOPY

Portable vibrational spectroscopy has become popular in the analysis of drug materials by law enforcement and drug checking services, as these techniques are rapid and non-destructive. There are two main vibrational spectroscopy techniques which have been explored for portable analysis of drug material; Fourier transform infrared (FTIR) and Raman spectroscopy.[36]

Infrared spectroscopy is based on the principle that chemical bonds in any molecule will be able to absorb infrared light if the dipole moment is changing during vibration. When infrared light is directed onto the sample, part of the light will be absorbed while the rest will pass through the sample. The absorbed light will produce a specific spectrum, which will be used to identify the functional groups present in the molecule. FTIR spectroscopy is normally used in conjunction with other techniques to aid in the identification of the chemical structure of any unknown substance.[36]

FTIR spectroscopy is also very suitable for use in the field since it is fast, non-destructive, relatively inexpensive, and requires minimal preparation of the samples. There are various techniques used in FTIR spectroscopy, which include transmission, attenuated total reflection, specular reflection, and diffuse reflectance spectroscopy. Of all these techniques, ATR spectroscopy is the most popular technique used in portable drug detection devices. In this technique, the infrared light is directed onto a dense crystal, which then produces an evanescent wave to penetrate into the sample in contact with the surface of the crystal.[37] Using ATR-FTIR it is possible to analyse and detect drugs like NBOMe and LSD when they are on blotter paper. Since blotter paper consists of both the drug itself and the paper matrix, the distinction between the signals from the drug itself and from the matrix may be difficult on some occasions. The technique can also be used to analyse drug samples in the form of powder, tablet or liquid by revealing the presence of harmful adulterants found in many street drugs.[38] The analytical capabilities of FTIR can be enhanced through the combination of FTIR data with statistical chemometric techniques such as multivariate curve resolution, principal component analysis, hierarchical cluster analyses, partial least squares discriminant analysis and support vector machines. These statistical tools can provide additional information about drug purity, provide assistance in recognising chemical type and simplify the interpretation of analytical results. For example, ATR-FTIR combined with a chemometric model has been used to differentiate between forms of cocaine as well as identify certain adulterants; such as caffeine, lidocaine and phenacetin. Similar techniques have also been used to estimate the concentration of fentanyl in complex mixtures and distinguish between different NBOMe-type compounds.[39] When utilized as a stand-alone drug detection technique, FTIR has certain drawbacks despite its benefits. Fentanyl and LSD are two examples of chemicals that the sensitivity might not be able to identify at very low amounts. Furthermore, the quality of the spectrum library supplied by the instrument manufacturer determines the accuracy of identification, and when analyzing complicated mixes, expert interpretation can still be necessary.[40]

Raman Spectroscopy is a tool that was first introduced by Raman and Krishnan back in 1928. The tool relies on the interaction between monochromatic light and molecules. When a laser beam is directed onto a sample, most of the scattered light has the same wavelength as the laser. This scattered light is then eliminated using filters. However, a

small amount of the scattered light has a slightly higher or lower frequency. This is due to the molecular vibrations. The tool has a number of advantages, which include speed, minimal preparation required, and the ability to analyze solids, liquids, or even packaged samples.[41] The tool can also be used on water samples because water has a weak Raman scattering. This has made portable Raman Spectrometers valuable tools for on-site chemical identification. The tool has been used for detecting drugs and dangerous substances. The tool ranges from small devices to pocket-sized devices.

Technological advancements like spatially offset Raman spectroscopy (SORS) lower the risk of exposure for analysts by enabling the analysis of substances through containers. Drugs like cocaine, amphetamine can be swiftly identified using Raman techniques, frequently in a matter of seconds.[42] However, fluorescence interference, which can mask weak signals, is a drawback of traditional Raman spectroscopy. A number of sophisticated methods, such as FT-Raman, resonance Raman, SORS, surface-enhanced Raman spectroscopy (SERS), and tip-enhanced Raman spectroscopy (TERS), have been developed to address these problems and increase sensitivity.[43] By adsorbing analytes onto rough metal surfaces like copper, silver, or gold, SERS greatly increases signal intensity and enables the identification of trace drug molecules. In order to better identify and quantify complex drug mixes, Raman data are also often integrated with chemometric algorithms like principal component analysis (PCA) and partial least squares (PLS).[44] Portable spectrometer is shown in Figure 2.

Figure 2: Portable Spectrometer.

MINIATURIZED MASS SPECTROMETRY

Mass spectrometry is a basic analytical tool recognized for its high sensitivity, selectivity, and ability to detect a wide range of molecules. Traditionally, mass spectrometers were bulky, sophisticated devices only suitable for use in a lab environment owing to their size and power demands.[45] However, with the recent advancements in technology, it has become possible to develop smaller, portable mass spectrometers, thus allowing chemical analysis to be conducted in the field or at the point of need. Portable mass spectrometers are developed through the use of sophisticated engineering techniques, which enable the reduction of the size and weight of the traditional mass spectrometers while ensuring good analytical performance. The key driver behind this progression was the increased requirement for real-time and on-location analytical capabilities.[46] Portable mass spectrometers are currently used in many fields including: environmental testing; drug manufacturing; forensic studies; and security. For instance, polluted areas (in air, water and

soil) now can be evaluated directly at the point of contamination; while drugs are monitored throughout their production to ensure their quality. The use of portable mass spectrometers in security and defense will also result in speedier identification of explosives, hazardous substances, and illicit substances. Compact parts, such as tiny ionization sources, mass analyzers, and sensitive detectors, are essential to miniaturized systems.[47] To produce ions from samples, methods like Laser Desorption/Ionization (LDI), Atmospheric Pressure Chemical Ionization (APCI), and Electrospray Ionization (ESI) are frequently employed. Various mass analyzers, including quadrupole, ion trap, and time-of-flight (TOF) analyzers, are employed based on the necessary speed and resolution. These devices can detect minuscule amounts of analytes thanks to sophisticated detectors and signal-processing techniques. By combining several functions onto tiny circuits, microfabrication technologies like photolithography and microelectromechanical systems (MEMS) have significantly contributed to the reduction of instrument size. There are still issues with power consumption, data management, and sample throughput even if portable mass spectrometers operate on par with many laboratory devices.[48] It is anticipated that advancements in artificial intelligence, materials science, and nanotechnology will further improve these gadgets. Portable mass spectrometry is expected to grow in importance as a tool for quick, on-site chemical research in a variety of scientific and industrial domains because to characteristics like wireless communication and automated data interpretation.[49]

Table 2: Portable Mass Spectrometry Components.[49]

Component	Examples	Function
Ionization source	ESI, APCI, LDI	Produces ions from analytes
Mass analyzer	TOF, quadrupole, ion trap	Separates ions by m/z
Detector	Electron multiplier, MCP	Detects ion signals

PORTABLE SEPARATION TECHNIQUES

Recent reviews have examined the use of portable separation techniques in forensic science and drug analysis, highlighting the growing importance of compact analytical instruments for identifying illicit substances. Portable systems offer the advantage of performing rapid testing directly in the field.[50] Generally, chromatography methods offer better separation efficiency than methods such as ion mobility spectrometry (IMS) and capillary electrophoresis (CE), although they are more difficult to miniaturize.[51] To overcome this difficulty, chromatography methods are coupled with miniaturized MS methods for better detection sensitivity. For example, GC-MS methods have been employed for drug checking activities aimed at detecting highly potent synthetic opioids such as fentanyl analogs, which might not be detected using test strips and other drug checking methods such as FTIR spectrometry. Similar methods have also been employed for detecting drugs and adulterants in seized samples, with results being compared with those obtained using conventional laboratory GC-MS methods for reliability. The detection of different illegal substances has also been assessed using portable capillary liquid chromatography (LC) with UV detection.[52] Some of these systems can be used remotely or in the field for both clinical and forensic screening because they run on internal batteries. Since the ratio of absorbance values can provide a more reliable signature than retention time alone, using detectors that measure absorbance at multiple wavelengths can further improve identification. Capillary electrophoresis (CE) is an additional quick separation method. It is also a technique that utilizes an electrical field to transport analytes through a capillary tube and utilizes only a small amount of the sample and reagents making CE applicable to miniaturized/miniaturized systems. CE can be coupled to a variety of detectors such as mass spectrometry or capacitively coupled contactless conductivity while remaining a possibility for portable drug testing.[53] Microchip electrophoresis has also shown promise for the on-site identification of illegal drugs which includes synthetic

cathinones in drugs seized from suspected dealers. However, further development is needed to optimize the use of CE for field use, particularly in situations where a sample must be prepared in advance (e.g., through derivatization). Figure 3 shows miniaturized TLC reader machine.[54]

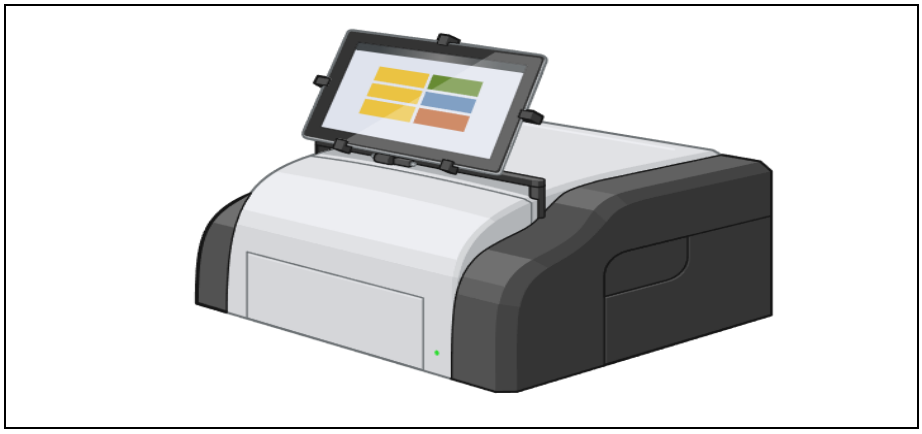

Figure 3: Portable TLC Reader.

ION MOBILITY SPECTROMETRY

Ion mobility spectrometry (IMS) is a highly sensitive method of detecting and analyzing chemical compounds present in various sample matrices without needing extensive sample preparation. Due to its high sensitivity, quick response, and ease of use, IMS is often utilized in security screening, such as in airports, correctional facilities, and customs, to screen drugs and explosive materials. Ion mobility spectrometry separates ions according to their velocity, which is driven by a low-intensity electric field.[55] Ions have different velocities, thus allowing them to be differentiated from one another. Sampling is done by swabbing a surface using a Teflon membrane connected to a sampling wand, which is then inserted into the spectrometer.[56] Other sample introduction techniques, such as sonic spray, have been researched, which is appropriate for use in security screening, especially due to its minimal equipment requirements. IMS has been effective in identifying a number of novel psychoactive substances (NPS), such as phenethylamines, cannabinoids, synthetic cathinones, and tryptamines. Because substances like synthetic cannabinoids are frequently applied to paper or other materials that are challenging to analyze using other techniques, it is especially useful in prison drug monitoring.[57] IMS can effectively identify a number of synthetic cannabinoid compounds, including recently discovered ones, according to studies using drug-infused papers from prisons. However, confirmatory laboratory analysis and frequent updates to spectral libraries are required due to the dynamic nature of NPS. IMS has certain drawbacks despite its benefits. Selectivity may be impacted by the method's inability to differentiate between substances with strikingly similar chemical structures.[58] Ion mobility can also be influenced by environmental variables like temperature and humidity, which could change analytical results in field settings. However, even for drug mixes, detection sensitivity can be increased by modifying instrument settings. In order to increase identification accuracy and decrease false positive or false negative results, IMS is frequently employed as a screening technique in conjunction with mass spectrometry.[59]

Table 3: Comparison of Portable Analytical Techniques[60]

Technique	Principle	Sample Type	Advantages	Limitations	Typical Applications
Colorimetric tests	Chemical reaction producing color change	Powders, tablets	Low cost, simple	Low selectivity	Preliminary drug screening
ATR-FTIR	Infrared absorption of functional groups	Solids, liquids	Rapid, non-destructive	Lower sensitivity for trace drugs	Drug identification
Raman spectroscopy	Light scattering from molecular vibrations	Solids, liquids, through packaging	No sample prep	Fluorescence interference	Field drug detection
IMS	Ion drift in gas under electric field	Swabs, surfaces	Very sensitive	Limited selectivity	Security screening
Portable MS	Mass-to-charge ratio of ions	Various matrices	High sensitivity	Higher cost	Confirmatory analysis

Table 4: Advantages And Limitations Of Portable Techniques.[60]

Technique	Major Advantages	Key Limitations
Colorimetric tests	Cheap, fast, easy to use	False positives
FTIR	Non-destructive, rapid	Limited sensitivity
Raman	Can analyze through packaging	Fluorescence interference
IMS	Very sensitive, quick screening	Poor differentiation of similar compounds
Portable MS	High accuracy and sensitivity	Expensive and complex

CONCLUSION

Analytical gadget shrinking has been considerably aided by developments in additive manufacturing and 3D printing. These technologies make it possible to create small, portable, and effective devices for applications including food safety, medical diagnostics, and environmental monitoring. These systems are particularly helpful in environments with limited resources because they are simple to set up and need little electricity. Additionally, by lowering solvent use, sample consumption, and energy requirements while enabling customizable and on-demand analytical instrument production, miniaturized chromatography and additive manufacturing complement the tenets of Green Analytical Chemistry (GAC). Forensic labs, law enforcement organizations, research centers, and drug-checking services all regularly conduct drug analyses. The goal of recent technology advancements is to translate the capabilities of complex laboratory instruments to field-useable portable devices. Because of their affordability and ease of use, traditional colorimetric drug tests have long been utilized for first identification. Microfluidic devices and smartphone-based colorimetric analysis are examples of contemporary methods that enhance the objectivity of results and enable the execution of several tests on a single device. However, because to their weak selectivity, these tests continue to be mostly used as screening techniques.

ATR-FTIR and Raman spectroscopy are examples of portable spectroscopic methods that offer quick, non-destructive analysis with little sample preparation. These techniques can even predict medication concentrations in complicated combinations when paired with spectral libraries and chemometric analysis. While surface-enhanced Raman spectroscopy (SERS) increases detection sensitivity, advanced Raman techniques, such as spatially offset Raman spectroscopy (SORS), enable drug identification through packaging.

When paired with straightforward swab sampling, portable mass spectrometry—especially ambient ionization methods like paper spray ionization (PSI-MS)—allows for the direct identification of drugs at extremely low concentrations and

is ideal for field testing. Because it is simple to use and efficient for identifying drugs and explosives in complicated samples, ion mobility spectrometry (IMS) is also frequently utilized in field settings.

Additionally, smaller mass spectrometers can be used in conjunction with portable chromatography and capillary electrophoresis equipment to improve drug molecule separation and identification outside of the lab. Customs and border agencies also analyze suspicious items using non-destructive methods including X-ray diffraction (XRD). With the exception of immunoassays, most emerging sensing technologies, such as optical and electrochemical biosensors, have not yet been fully developed into commercial field-ready devices, although they show promise for quick and sensitive drug detection.[60]

ABBREVIATIONS

XRD: X-ray diffraction

IMS: Ion mobility spectrometry

PSI-MS: Paper spray ionization-mass spectrometry

SORS: Spatially offset Raman spectroscopy

SERS: Surface-enhanced Raman spectroscopy

ATR-FTIR: Attenuated Total Reflectance- Fourier Transform Infrared Spectroscopy

GAC: Green Analytical Chemistry

NPS: Novel psychoactive substances

CE: Capillary electrophoresis

LC: Liquid chromatography

GC-MS: Gas Chromatography-Mass Spectrometry

MEMS: Microelectromechanical systems

TOF: Time-of-flight

ESI: Electrospray Ionization

APCI: Atmospheric Pressure Chemical Ionization

LDI: Laser Desorption/Ionization

PCA: Principal component analysis

PLS: Partial least squares

TERS: Tip-enhanced Raman spectroscopy

SERS: Surface-enhanced Raman spectroscopy

LSD: Lysergic acid diethylamide

NBOMe: N-(2-methoxybenzyl) (NBOMe) derivative of LSD

RGB: Red, green, blue

LOC: Lab-on-chip

PDMS: Polydimethylsiloxane

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