



High-throughput platforms for microextraction techniques

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Abstract

The proposal of high-throughput platforms in microextraction-based approaches is important to offer sustainable and efficient tools in analytical chemistry. Particularly, automated configurations exhibit enormous potential because they provide accurate and precise results in addition to less analyst intervention. Recently, significant achievements have been obtained in proposing affordable platforms for microextraction techniques capable of being integrated with different analytical instrumentations. Considering the evolution of these approaches, this article describes innovative high-throughput platforms that have recently been proposed for the analysis of varied matrices, with special attention to laboratory-made devices. Additionally, some challenges, opportunities, and trends regarding these experimental workflows are pointed out.

Keywords Microextraction · High-throughput analysis · Sample preparation · Automation

Introduction

The development of rapid, efficient, and straightforward methodologies consists of important demand in Analytical Chemistry. In particular, the evolution of modern and sophisticated analytical instruments has significantly contributed to enhancing sensitivity and robustness of chemical analysis. However, in most cases, a sample preparation step prior to instrumental analysis is required because of matrix complexity and/or low concentration of the target analytes [1].

Sample preparation is extremely important for successful analytical methodologies, and it is basically focused on reducing or eliminating some possible interfering components from sample matrix (cleanup), also allowing for the

concentration/enrichment of the target analytes before the instrumental analysis. Some experimental strategies are capable of providing those features simultaneously which is of particular interest to enhance analysis throughput. However, this step is generally laborious, time-consuming, and typically performed with the use of extraction techniques such as liquid–liquid extraction (LLE) and solid-phase extraction (SPE). In general, these techniques exhibit formidable extraction efficiency for a wide range of analytes in different aqueous matrices. Interestingly, SPE has also been proposed as in-line/on-line systems in which high-throughput analysis can be achieved. In this case, numerous devices manufactured by different companies can provide successive extractions using fully automated workflows typically interfaced with liquid chromatography. Conditioning, washing and elution steps can be performed automatically, and some instruments also permit to extract one sample while another is being analyzed by liquid chromatography. This configuration can provide high precision and accuracy, as well as reduced risks of contamination and loss of analyte [2].

On the other hand, these classical sample preparation techniques possess some significant limitations particularly related to the use of large amounts sample and toxic organic solvents. LLE approaches can also be affected by the formation of emulsions which may decrease the extraction efficiency. Moreover, in some cases, costs of SPE cartridges may hinder the application of this technique [3, 4]. For many years, sample preparation techniques have

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been overlooked with quite low interest of the scientific community. However, this situation rapidly changed in the 1990s and 2000s with remarkable developments of microextraction techniques such as solid-phase microextraction (SPME) and different configurations of liquid-phase microextraction (LPME). These techniques have been proposed to circumvent some drawbacks of classical techniques such as LLE and SPE. Therefore, most of these sustainable techniques are in accordance with the modern concepts of Green Analytical Chemistry (GAC) and with the recent introduced concept of White Analytical Chemistry (WAC) in which a balance between sustainability and functionality is considered [5, 6].

The progress of microextraction techniques through the years is consistent, and novel configurations and devices have been suggested and evaluated for specific applications. In general, these techniques feature high extraction and pre-concentration capabilities, sustainable aspects, affordable, and versatile configurations. In addition, significant number of configurations are capable of being automated to provide high-throughput analysis. Particularly, less user intervention and high sample throughput are often required also for routine laboratories in many research areas. These factors can reduce sample manipulation enhancing the method reproducibility with the development of specific platforms that can be coupled or interfaced with analytical instrumentation. However, some challenges have been faced since these platforms may require special configurations [4]. Numerous analytical strategies were developed by interfacing sustainable microextraction techniques with platforms that allow for processing large number of samples. It is worth mentioning that, in the last years, the pandemic forced millions of people to work from home. Therefore, more independent analytical platforms with less user intervention and possibility of being controlled by remote access have been stimulated.

Additionally, remarkable progress has been achieved with robotic-assisted configurations. In general, the use of commercial robotic-assisted devices in sample preparation coupled to chromatographic techniques can significantly increase the instrumentation costs. Commercial instruments specifically dedicated to providing full automation of sample preparation procedures exhibit formidable results; however, the sophisticated configuration is limited to a few laboratories worldwide. Recently, alternative possibilities of automated and high-throughput robotic-assisted microextractions have been proposed [7]. Importantly, affordable materials and user-friendly technologies such as 3D-printing are gaining attention for the development of specific devices for sample preparation procedures. In this case, lab-made platforms are being developed with focus on device manufacturing and low-cost electronic controllers. Moreover, microfluidic devices have also been investigated to deliver high-throughput microextraction approaches.

Regarding analytical platforms, the use of 96-well plate systems in sample preparation offered novel and valuable possibilities for the automation of analytical methodologies. Importantly, analysis throughput can be significantly enhanced using these approaches since multiple samples can be processed simultaneously. Therefore, sustainable, versatile, and robust methodologies can be achieved [8].

The aim of this article is to highlight some recent achievements and trends in high-throughput methodologies based on microextraction techniques with particular interest to studies reported in the last 5 years. Experimental strategies based on solid and liquid extraction phases, membranes, and electro-mediated apparatus are mentioned and briefly discussed. In addition, opportunities, challenges, and future directions in this field are pointed out. These trending studies are separated by technique to provide a more comprehensive understanding of each experimental strategy.

Solid-phase microextraction (SPME)

Solid-phase microextraction is a popular and well-established technique developed in 1990 [9] that is constantly being improved to provide high-throughput workflows. Alternative configurations were proposed to enable preparation of multiple samples simultaneously by coupling SPME fibers with 96-well plate platforms [8]. In this case, the development of different configurations such as thin film microextraction (TFME) [10] and in-tip-SPME [11] significantly contributed to offer straightforward and high-throughput methodologies.

High-throughput SPME-based protocols to analyze complex matrices have evolved through the years. Approaches using coated-blade spray (CBS) are gaining attention because they exhibit numerous advantages compared to classical extraction protocols including short analysis time, reduced solvent consumption, and low human intervention. Considering these features, the use of CBS directly coupled to mass spectrometry (MS) was proposed [12]. In this configuration, a 96-well plate CBS holder assembly comprised of blades coated with hydrophilic-lipophilic balance (HLB) particles was used for the extraction of pesticides from juice samples and drugs of abuse from urine. In this configuration, the coating length used was 10 mm, and thickness was 10 μm . Additionally, a 12-blade autosampler was systematically developed based on a stepper motor to permit movements of those blades before the introduction of the sample in MS. After the extraction step, solvent is added to the blades, followed by the application of electrical potential before the MS analysis. Moreover, this automated configuration can dramatically increase sample throughput for the analysis of multiple samples, and it exhibits tremendous potential for screening purposes. Figure 1 shows a scheme

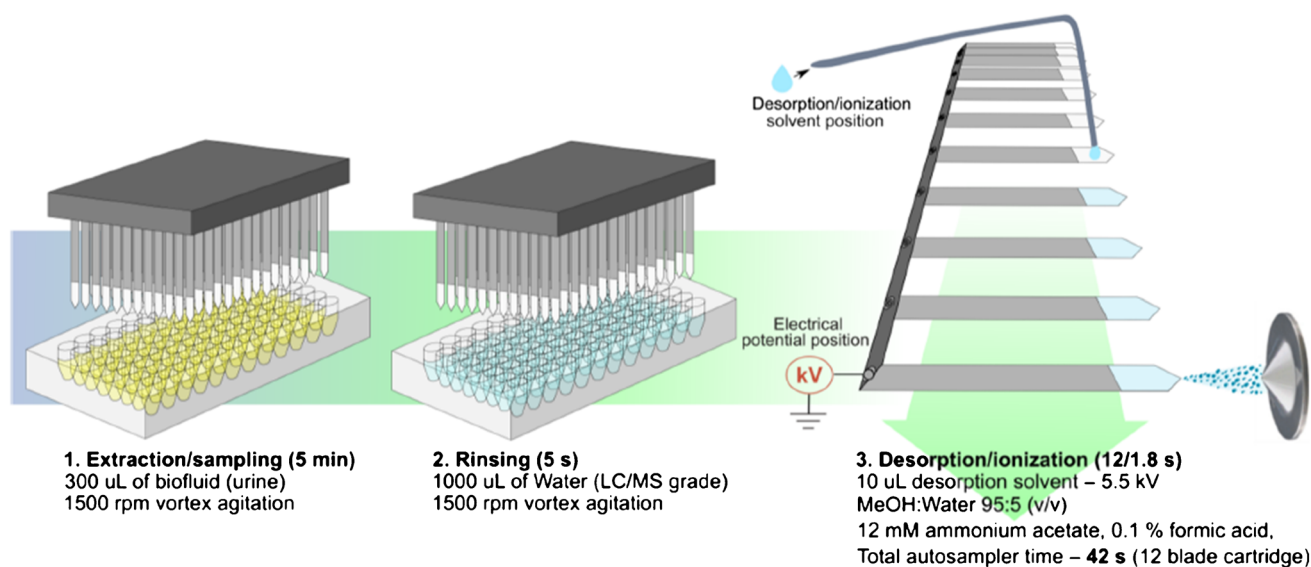


Fig. 1 Coated-blade spray (CBS) coupled to MS. Reproduced with permission from [12]

of the CBS experimental workflow integrated to mass spectrometry inlet.

More recently, the use of SPME for multiple extractions has also been proposed for the analysis of complex biological samples such as human plasma [13]. In this case, drugs capable of binding to plasma were determined since estimating free concentration of some drugs in blood can provide valuable information in therapeutic drug monitoring. Particularly, a device comprised of a polypropylene 96-pin platform employing a 5- μm layer of C_{18} -coated solid phase combined with biocompatible polyacrylonitrile polymeric adhesive was suggested. The length of the pins was 24.7 mm, and the diameter of a bare pin tip is 1 mm. Using this configuration, the extraction platform was fully automated by integrating with a Concept96 system allowing for a high-throughput approach. Additionally, very satisfactory sample cleanup associated with accurate determination of pharmaceuticals were obtained using LC–MS/MS.

Following some recent trends in environmentally friendly methodologies, the proposal of biosorbents as extraction phases in TFME approaches is also gaining attention. Biosorbents consist of macromolecules containing numerous functional groups capable of interacting with the analytes through different mechanisms such as sorption, ion exchange, and complexation. These materials are natural, biodegradable, and renewable which is important to enhance the sustainability and “greenness” of the analytical methodology [14]. Specifically, cork [15], bract [16], and recycled diatomaceous earth [17] have been successfully employed as sorbent phases in high-throughput TFME approaches coupled to 96-well plate systems. In all cases,

the sorbent phase is easily attached to the pins using double sided adhesive films. High extraction efficiency, adequate mechanical and chemical stability, and long coating lifetime with no significant carryover are the main analytical advantages of these materials. In addition to that, these affordable devices are very attractive for research laboratories worldwide with possibility of application also in complex samples.

Polyamide noncoated device for adsorption-based microextraction (PANDA)

The evolution of solid materials specifically designed and applied for sample preparation is enormous [18]. In this case, novel strategies have been described to produce metal organic frameworks (MOFs) [19], magnetic nanoparticles (MNPs) [20], molecular imprinted polymers (MIPs) [21], among others. Interestingly, 3D-printing has recently been exploited as affordable and versatile technique to create novel classes of solid materials capable of being exploited in high-throughput approaches.

Polyamide noncoated device for adsorption-based microextraction (PANDA) consists of a very recent and biocompatible 3D-printed ready-to-use analytical platform comprised of carbon fiber reinforced polyamide biocomposites [22]. This configuration is based on a series of pins similar to TFME; however, PANDA features faster preparation, less waste generation, and reduced production costs. The first approach of this microextraction technique employed a solid support formed by polyamide 6 and carbon fiber 15%

that was ready-to-use after prototyping, requiring only a brief postprocessing step. This microextraction technique was successfully used for the determination of molecules of diverse chemical natures in oral fluid by LC–MS/MS. It worth mentioning that extraction of the analytes is carried out directly by adsorption on the surface of the pins without requiring any additional coating material.

This novel and high-throughput microextraction platform offers numerous advantages associating sustainable analytical aspects combined with the high versatility of 3D-printing. Certainly, other alternative methodologies based on PANDA concept will be proposed in the next years due to the potential and greenness of this straightforward sample preparation approach.

Slug-flow nanoextraction (SFNE)

The proposal of high-throughput analytical methodologies that require volumes of organic solvents at nanoliter scale is also a trend in sample preparation. However, downscaling liquid phase microextractions to nanoliter volumes consists of a significant challenge in any experimental workflow.

A remarkable development was reported in 2020, and it consists of slug-flow nanoextraction (SFNE) [23]. This approach is based on droplet microfluidics that allow multiple liquid–liquid extractions to be performed simultaneously in a capillary tube. Particularly, this approach requires only 5 nL of sample and organic solvent that are pumped through the tube by a syringe pump. In this study, a 25 μ L syringe with a 15–30 cm length of 100 μ m inner diameter (i.d.) 360 μ m outer diameter (o.d.) was used. Sample and solvent plug pairs are juxtaposed in a tube with each pair separated by an immiscible oil. Therefore, the extraction procedure is performed when the pairs flow through the tube. As a proof of concept, octanol–water partition coefficients of some analytes were determined by online coupling this experimental setup with UV detection. Furthermore, SFNE was combined with ESI–MS/MS for the determination of some drugs in plasma and urine samples. Using this configuration, high-throughput analyses were achieved with 60 extractions performed within 5 min. On the other hand, some drawbacks were observed in mass spectrometry analysis particularly related to the compatibility of the extraction solvent used in SFNE procedure.

Membrane-based approaches

The use of membranes in microextraction techniques was firstly proposed in 1999 by employing polypropylene hollow fibers supported with 1-octanol to analyze biological fluids. Initially, this configuration was

termed liquid–liquid–liquid microextraction [24] and allowed for efficient extractions in complex matrices. This configuration has also been permitting a number of variations and versatile experimental setups capable of being automated. In particular, trends in high-throughput membrane-based approaches involve coupling with 96-well plate platforms as well as proposal of microfluidic devices.

In general, the proposal of coupling membranes with 96-well plate systems involves the use of a series of pins in which small pieces of polypropylene hollow fibers are inserted. Generally, an organic solvent is immobilized into the membrane pores (supported liquid membrane) and immersed in the samples for the extraction process. A promising trend is based on concepts of hollow-fiber renewable liquid membrane extraction (HFRLM) consisting of adding a small volume of organic solvent into the sample to renew the liquid membrane. In this case, up to 96 samples can be processed simultaneously with low analyst intervention. This semi-automated approach allowed for the efficient determination of cocaine and metabolites in urine samples with analysis performed by LC–QTOF–MS [25]. Figure 2 shows the steps of the experimental procedure of this analytical platform that permitted significantly higher analysis throughput in comparison with traditional HF–LPME approaches.

The use of sustainable solvents such as deep eutectic solvents (DESs) coupled to membrane-based configurations also consists of a recent trend in sample preparation. Significant attention has been devoted to DESs because they feature important advantages such as biodegradability, satisfactory chemical stability, and simple preparation. The use of these sustainable solvents immobilized into the porous of small pieces of polypropylene membranes coupled to 96-well plate platforms has been recently proposed to determine emerging pollutants in aqueous samples. This approach consists of a straightforward and versatile strategy capable of being automated [26]. In this case, greener methodologies can be obtained since toxic organic solvents are not required for extracting the analytes. However, the performance of this approach in more complex matrices still need to be evaluated.

Additionally, a membrane-based approach termed parallel artificial liquid membrane (PALME) is also capable of being combined with 96-well plate systems. In this approach, the aqueous acceptor solution and the aqueous sample are separated by a flat membrane supported with organic solvent. A series of flat membranes can be easily placed in a multiwell platform. Considering the recent trends toward greener analytical methodologies, sustainable solvents have been evaluated in this high-throughput approach. Very recently, a coumarin/thymol-based

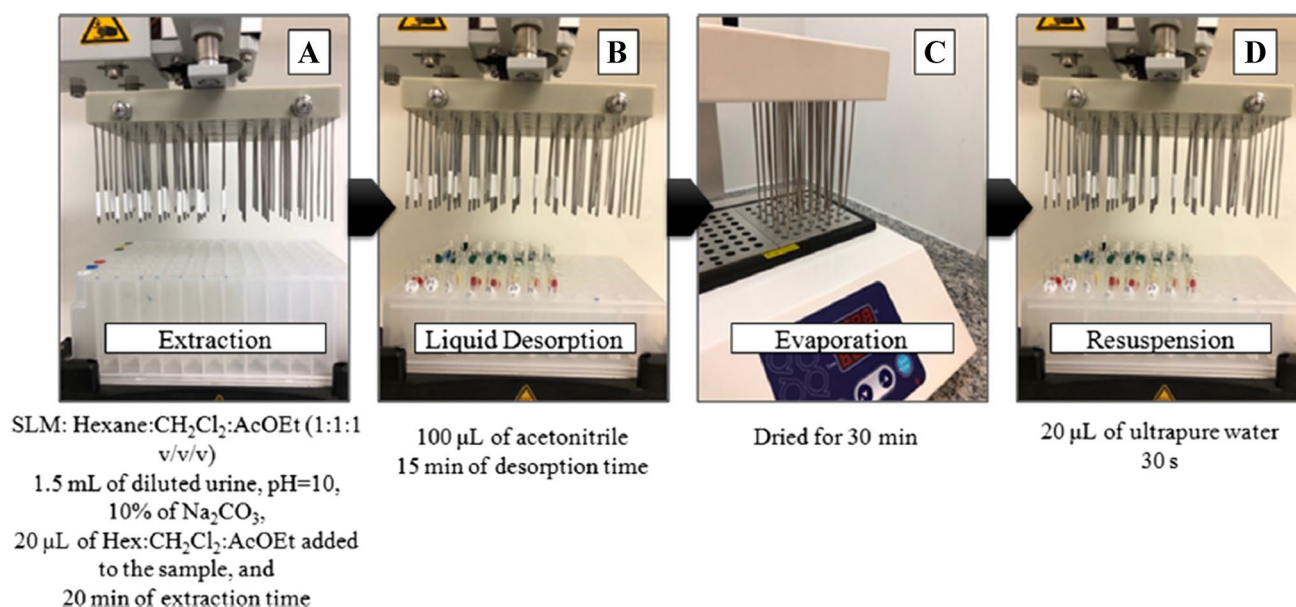


Fig. 2 Hollow-fiber renewable liquid membrane extraction (HFRLM) coupled to 96-well plate platform. Reproduced with permission from [25]

deep eutectic solvent has been examined to replace toxic organic solvents generally used [27]. In this case, successful determination of acidic polar nerve agent degradation products by LC–MS/MS was achieved with 196 samples prepared within 120 min using PALME-based extraction platform.

Another membrane-based configuration that is being improved consists of electromembrane extraction (EME) [28]. In this procedure, an electric field is used between the donor and acceptor phases to increase the extraction kinetics of ionized analytes through a supported liquid membrane [29]. In a recent study, a fully automated μ -EME procedure consisting of programmable-flow-based mesofluidic platform was proposed for the determination of nonsteroidal anti-inflammatory drugs in urine and wastewater samples [30]. In this case, a liquid membrane is formed as a plug of organic solvent, which is sandwiched between the donor and acceptor solutions inside of a thin fluorinated ethylene polypropylene tubing. This innovative strategy was online coupled to HPLC–UV allowing for enhanced sample throughput compared to classical EME approaches. Besides that, the membrane has been constantly renewed during the extraction cycles, and sequential injection analysis (SIA) was configured to perform a “heart-cut” injection of the acceptor solution in the HPLC–UV. In this configuration, μ -EME was performed in chemically inert FEP tubing (1.6 mm ID and 3.2 mm OD). Features such as very low solvent and sample consumption (only few microliters), possibility of unattended operation, and online hyphenation with

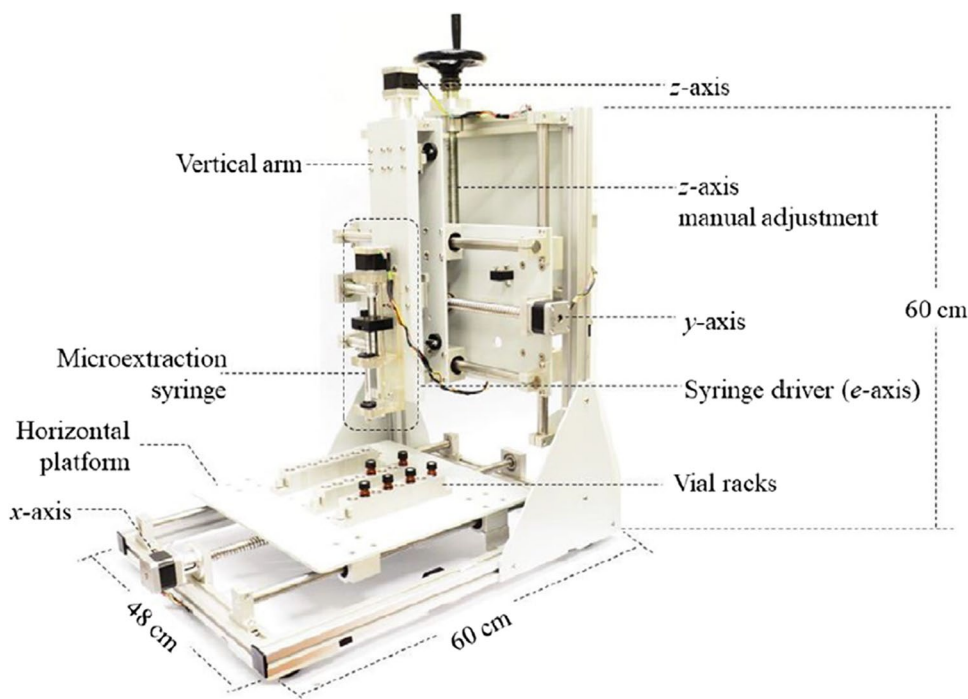
analytical instruments make this platform an interesting option to be explored and improved in next years.

Lab-made robotic-assisted extraction platforms

An important milestone to increase the sample throughput in microextraction approaches was proposed in 2019 with the development of an open-source multi-purpose cartesian robot [7]. This lab-made device is capable of performing all steps of sample preparation workflow; additionally, the platform can be online hyphenated with analytical instrumentation (i.e., liquid chromatography coupled to mass spectrometry). Basically, the system is based on Arduino-controlled xyz cartesian robot equipped with a micro-syringe driver capable of performing all steps required in liquid-based microextraction strategies. Successful applications have been reported for SDME and HF-LPME configurations with high precision and accuracy [31, 32]. The lab-made automated platform containing the device dimensions is shown in Fig. 3.

A possible trend in robotic-assisted platforms for microextraction is related to developing specifically designed 3D-printed components. Considering the potential and versatility of 3D-printing technology, it is expected the development of numerous platforms that can be further integrated with low-cost electronic controllers such as Arduino.

Fig. 3 Platform based on Arduino-controlled xyz cartesian robot. Reproduced with permission from [7]



In addition, microextraction by packed sorbent (MEPS) is another important configuration based on solid extraction phases that has been recently automated for increasing sample throughput. Advantages of applying MEPS include low sample and solvent consumption, as well as different possibilities of on-line and off-line automation [33–35]. Recently, an open-source robotic platform based on a lab-made multi-syringe autosampler has been coupled to MEPS for the determination of cannabinoids in human urine prior to LC–MS/MS [36]. Furthermore, this study also exploited the development of an alternative sorbent (molecular imprinted polymer) for the extractions. In general, commercially available syringes for MEPS are comprised of extraction phases similar to those used for SPE. Therefore, the possibility of developing alternative sorbents is important to expand the applicability for specific classes of analytes. This configuration also permitted the use of multiple syringes simultaneously which dramatically decreased the manual labor for the extraction/desorption procedures. Due to the versatility and simple application, MEPS exhibits enormous potential to be used in forensic and clinical determinations. For these reasons, this high-throughput platform may offer alternatives in numerous laboratories.

Microfluidic and mesofluidic platforms

The use of 3D manufacturing to create microfluidic platforms has emerged as powerful strategy to systematically design apparatus for sample preparation approaches. In

general, methodologies that employ microfluidic platforms exhibit higher sample throughput compared to traditional methodologies for sample preparation. Therefore, a cascade of possibilities and applications can be exploited using these configurations.

In particular, the analysis of complex samples consists of an important challenge, and a more detailed sample preparation step need to be performed prior to instrumental analysis. In order to circumvent some limitations obtained with traditional sample preparation techniques, a 3D-printed microfluidic device produced using fused deposition modeling has been proposed for the analysis of petroleum [37]. In this case, a sample preparation step based on μ SPE was successfully performed in 3D-printed microchips prior to GC–MS and GC \times GC-FID. Dimensions of microchips were 25 mm \times 50 mm of base and 10 mm of height. This versatile approach permitted a tenfold reduction in sample preparation time compared to reference method; moreover, the extraction platforms have shown satisfactory chemical and mechanical stability emphasizing the great potential of 3D-printing for proposing novel and alternative high-throughput configurations.

Additionally, possibilities of employing 3D-printing in lab-on-a-valve (LOV) methodologies also consist of an important trend [38]. In a proof-of-concept study, stereolithography was used for producing unibody transparent mesofluidic platforms coupled with on-chip electrochemical or optical detection for varied applications including analysis of complex samples using μ SPE. This

approach allowed for high-throughput/automatic analysis with fast and inexpensive prototyping of multipurpose microfluidic platforms.

Experimental configurations using magneto-active solvents

The development of alternative solvents that can be applied in microextraction approaches is a hot topic in analytical chemistry. Proposal of magneto-active solvents such as magnetic ionic liquids (MILs) [39, 40] and magnetic deep eutectic solvents (magnetic-DES) [41, 42] is offering numerous alternatives to replace toxic organic solvents. In particular, MILs have been recently exploited as extraction phases combined with 96-well plate platforms. These solvents exhibit high chemical stability, multiple solvation capacity, tunable chemical structure, and strong response when subjected to external magnetic fields. It is worth mentioning that MILs are neat solvents with a paramagnetic component within the chemical structure. Therefore, they can be easily recovered from the sample solution using a magnet. This feature opens novel possibilities to be exploited in high-throughput approaches.

The first platform based on MILs coupled to 96-well plate system was proposed in 2019 and termed parallel-single drop microextraction (Pa-SDME) [43]. This high-throughput configuration is comprised of a series of rod magnets attached to the pins of a lab-made 96-pins platform. In this approach, MILs permitted additional drop stability for a SDME procedure due to the magnetic

properties of these compounds. In consequence, up to 96 samples can be processed simultaneously after suspending a small drop of MILs in the tip of each rod magnet. The extraction procedure was performed by immersing the $[P_{6,6,6,14}^+]_2[MnCl_4^{2-}]$ MIL in the sample solution, followed by solubilization of the analyte enriched MIL in acetonitrile and injection in HPLC–DAD. A scheme of the extraction apparatus is shown in Fig. 4. Pa-SDME proved to be efficient for the determination of environmental pollutants in water samples.

This magneto-based configuration was also successfully employed in dispersive liquid–liquid microextraction (DLLME) for the analysis of urine [44]. Moreover, in situ generation of the $[Co(C_4IM)_4^{+2}]_2[NTf_2^-]$, $[Ni(C_4IM)_4^{+2}]_2[NTf_2^-]$, and $[Ni(BeIM)_4^{+2}]_2[NTf_2^-]$ MILs was capable of producing extraction phases for a parallel dispersive droplet extraction approach (Pa-DDE) [45]. In this case, a 96-well plate system consisting of a set of magnetic pins was able to recover the hydrophobic MIL droplets after in situ formation. This configuration provided successful extraction of environmental contaminants in aqueous samples.

These MIL-based approaches feature high extraction capacity permitting direct injection in HPLC instruments after the extraction and solubilization steps. This compatibility with liquid chromatography is important to avoid back-extraction steps prior to instrumental analysis. On the other hand, some limitations have been observed in gas chromatography for the direct injection of MILs; in this case, thermal desorption using a special unit prior to sample injection can be useful.

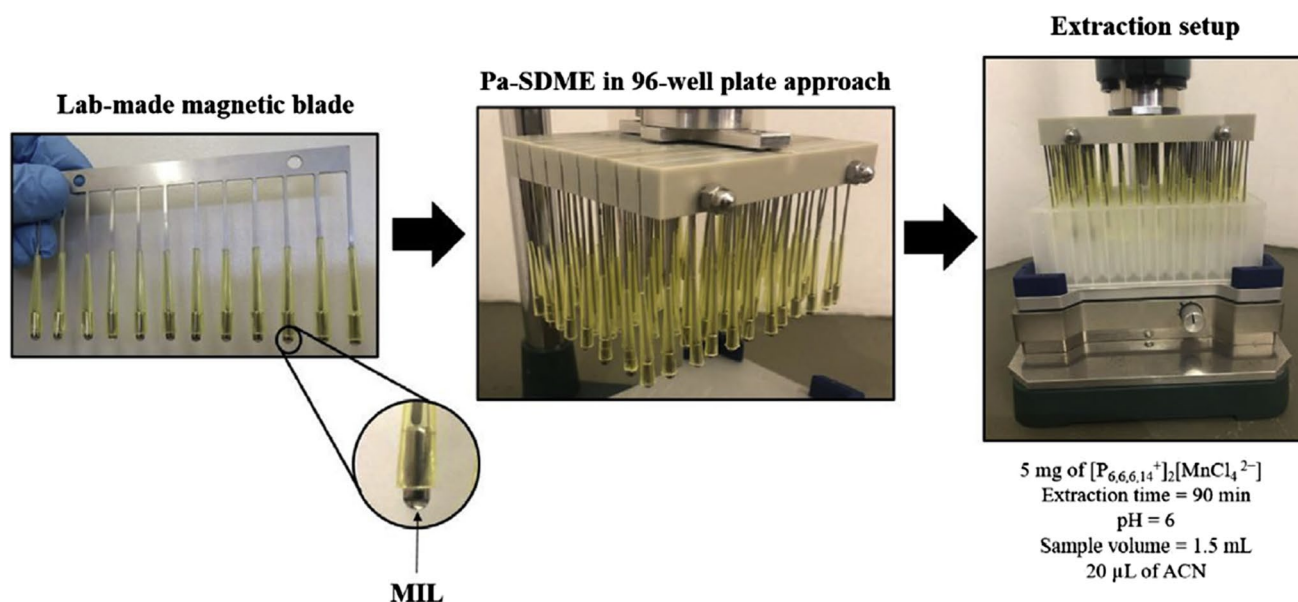


Fig. 4 Pa-SDME using magnetic ionic liquids as extraction phases. Reproduced with permission from [43]

Table 1 Features of the high-throughput approaches discussed in this study

Sample preparation technique	Analytes	Matrix	Instrumental technique	Total extraction time	Number of samples processed simultaneously	LOQ (ng mL ⁻¹)	Ref
Coated blade spray (CBS)	Drugs of abuse and pesticides	Human urine and apple juice	Mass spectrometry	5 min	12 (capable of being processed up to 96)	0.5–10	[12]
SPME	Drugs	Human plasma	LC-MS/MS	10–40 min	Up to 96	-	[13]
TFME	Emerging contaminants	River water	HPLC-DAD	180 min	Up to 96	0.8–15	[15]
TFME	Estrogens	Human urine	HPLC-FD	150 min	Up to 96	1.0–10	[16]
TFME	Endocrine disrupting compounds	River water	HPLC-DAD	240 min	Up to 96	5.0–25	[17]
PANDA	Drugs	Oral fluid	HPLC-MS/MS	150 min	Up to 96	1.0–5	[22]
SFNE	Drugs	Human plasma, synthetic urine (SU), and artificial cerebral spinal fluid (aCSF)	Mass spectrometry, UV, or laser-induced fluorescence (LIF)	≈ 5 s	-	1.9–16	[23]
HFRLM	Drugs of abuse	Human urine	LC-QTOF-MS	35 min (extraction and desorption)	Up to 96	5.0–50	[25]
HF-MMLLE	Environmental contaminants	Tap and stream water	HPLC-DAD	65 min (extraction and desorption)	Up to 96	1.0–20	[26]
PALME	Alkyl methyl phosphonic acids (AMPAAs)	Human urine	LC-MS/MS	120 min	Up to 96	0.04–5.35	[27]
μ-EME	NSAIDs	Urine and influent wastewater	HPLC-PDA	10 min	-	100–2300 ^a	[30]
Robotic-assisted SDME	Pesticides	Coconut water samples	LC-UV and LC-MS	10 min	-	0.25	[31]
Robotic-assisted dynamic SDME	Parabens	Wastewater	LC-MS	20 extraction cycles of 90 s	-	0.30 ^a	[32]
Automated MIP-MEPS	Cannabinoids	Human urine	LC-MS/MS	-	Up to 6 MEPS syringes	5.2–20	[36]
μSPE using 3D-printed device	Untargeted analysis	Petroleum	GC x GC-FID, GC-MS, ¹ H NMR and FT-ICR MS	-	-	-	[37]
3D-μFIA – based on Lab-on-a-valve concept	Glucose, metals, phospholipids, and bromothymol blue	Serum, soil, artificial biological and food samples	ICP – OES, Electrochemical and spectrophotometric detections	-	-	-	[38]
Pa-SDME	Environmental contaminants	Water samples	HPLC-DAD	90 min	Up to 96	5.0–10	[43]
Pa-SDME	Pesticides	Human urine	HPLC-DAD	130 min	Up to 96	25	[44]
In situ Pa-DDE	Environmental contaminants	Water samples	HPLC-DAD	75 min	Up to 96	25	[45]
SPME based on 3D-printed sorbent	Steroids	Human plasma	LC-MS	75 min	Up to 96	-	[46]

^aLimit of detection (LOD)

CBS, coated blade spray; SPME, solid-phase microextraction; TFME, thin-film microextraction; PANDA, polyamide noncoated device for adsorption-based microextraction; SFNE, slug-flow nonextraction; HFRLM, hollow fiber renewal liquid membrane; HF-MMLLE, hollow fiber—microporous membrane liquid–liquid extraction; PALME, parallel artificial liquid membrane extraction; EME, electromembrane extraction; SDME, single drop microextraction; MIP-MEPS, molecularly imprinted polymer-microextraction by packed sorbent; Pa-SDME, parallel-single drop microextraction; Pa-DDE, parallel-dispersive droplet extraction; SPE, solid-phase extraction; FIA, flow injection analysis

In order to provide a comparison among the studies previously discussed, Table 1 contains some analytical features of the manuscripts highlighted in this study.

Outlook

Based on the significant milestones briefly discussed in this manuscript, it is worth mentioning that the design/development of high-throughput sample preparation platforms for microextraction approaches is continuously evolving. This field is expanding to provide reliable and affordable configurations that can be combined with different analytical instrumentation such as mass spectrometry, chromatographic, or electroanalytical methods.

Likewise, proposal of automating (fully or partially) analytical methodologies is also an important requirement. In the last years, due to the pandemic situation, numerous laboratories faced issues to offer their services. Therefore, efforts are expected in the next years to creating analytical methodologies and microextraction platforms capable of being remotely controlled. In this case, open-source platforms based on electronic devices are great options to be developed/enhanced, as well as proposal of microchip-based devices for the analysis of challenging matrices.

Evaluation of novel 3D-printed platforms will be explored due to the high versatility of this manufacturing strategy. Particularly, 3D-printed platforms integrated with electronic controllers comprised of inexpensive devices for automating experimental workflows can be more comprehensively examined. These platforms based on Arduino and other open-source codifications exhibit tremendous potential and numerous opportunities for application. Furthermore, high-throughput microextraction approaches in which the extraction devices are easily manufactured via 3D-printed and used as sorbent phase without any additional coating, as the recently reported strategy termed PANDA, consist of an open window to be exploited. Another recent configuration also has examined 3D-printed sorbents with a scabbard-like shape comprised of a commercial material (LAY-FOMM) capable of being integrated with 96-well plate systems [46]. Efforts to integrate these devices directly with mass spectrometry will be exploited to offer more straightforward analytical methodologies.

Additionally, magneto-active solvents such as MILs and magnetic-DES are gaining significant attention in multiwell-based experimental workflows. These solvents are easily manipulated with magnetic field, and proposal of novel and alternative configurations that allow for multiple extractions performed simultaneously will certainly be investigated.

High-throughput methodologies are required in numerous laboratories worldwide. In general, this feature can be obtained by automating the experimental workflows in order to increase the number of samples processed simultaneously or sequentially. Microextraction techniques can exhibit some challenges to be automated; however, impressive progress has been achieved and reported in the last years. This study offered a brief overview of some recent and important developments related to high-throughput platforms used for microextraction techniques. Some aspects of these platforms were mentioned and discussed, and trends in the development of high-throughput microextraction techniques were pointed out.

It is worth mentioning the importance of sample preparation within chemical analysis. Sophisticated analytical instrumentation can deliver excellent results in terms of accuracy, sensitivity, and precision; however, a sample preparation step is generally required to overcome issues relate to matrix complexity and concentration of the analytes. Importantly, proposal and evaluation of high-throughput and green sample preparation strategies are hot topics to be exploited in different matrices.

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Declarations

Conflict of interest The author declares no competing interests.

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