Review:

Recent Studies on Optical and Electrochemical Sensors for On-Site Detection of Methamphetamine

Hussain Alessa[1*] and Sulafa Jamal Mohammed Nassar

Department of Chemistry, Faculty of Science, Umm Al-Qura University, Makkah 24230, Saudi Arabia

* ***Corresponding author:***

email: hhessa@uqu.edu.sa

Received: September 29, 2025
Accepted: December 23. 2025

DOI: 10.22146/ijc.111577

Abstract: *Universally, the usage of unlawful drugs is one of the serious matters that reduces the prosperity and health of the users and communities. Methamphetamine (MAPA) is one of the illicit drugs that is fabricated in clandestine laboratories. It is considered one of the most harmful drugs spreading among youths around the globe. Therefore, the development of sophisticated sensing technology for its rapid and accurate detection is required. Sensors consist mainly of a recognition element, a transduction element and a signal processor for detecting MAPA and recording its chemical concentration. Different chemical sensors, such as optical, magnetic, thermal and electrochemical sensors have been utilized. They differ in the working mechanism and the type of measured signal. The aim of this review is to provide a summary of the up-to-date advancements in optical and electrochemical sensors that have been used for MAPA detection in different samples, particularly from 2012 to 2025.*

Keywords: *methamphetamine; sensors; voltammetry*

■ INTRODUCTION

N-methyl-1-phenylpropane-2-amine compound, known as methamphetamine (MAPA), is one of the popular illegal drugs worldwide. MAPA ($C_{10}H_{15}N$, Fig. 1), with a molecular weight of 149.24 g/mol, is synthesized from ephedrine [1-2]. MAPA is known by different nomenclature like meth, crystal meth and whiz. It has two isomers named dextro (*d*-) and levo (*l*-). MAPA is a basic drug with a pKa of 9.9; it is usually extracted in basic media by organic solvents [3]. Although MAPA has been used for the short-term treatment of extravagant obesity and hyperactivity disorder, it may cause unpleasant addiction strengthened by its euphoric feeling [4]. MAPA found popularity among young people as it stimulates their pleasure by increasing the release of dopamine and serotonin, which works by blocking certain receptors in the brain. However, the consumption of higher MAPA amounts would result in high blood pressure, breathing difficulty, paranoia, uncontrollable violence and death [4-7].

The transfer of MAPA from mothers to their infants has not been proven yet, as it has no correlation with

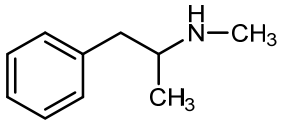


Fig 1. The structure of MAPA

maternal depression [8]. Some psychotropic effects would increase directly or indirectly by using MAPA, such as decreases driving ability leading to car accidents, extreme violence, spreading contagious diseases, simplify sexual assaults, air pollution by the released smoke, reduces the safe vegetation and converting it to illegal drug cultivation, so the release of MAPA and its metabolites into the wastewater affect the water treatment processes and thereby the final water quality [6,9-10]. MAPA is produced by different approaches, such as by Leuckart and Nagai method [11-12], phenyl-2-propanone method [13], red phosphorus method [14], one pot method [15]. It can also be produced illegally and used via different routes; it can be injected, inhaled, smoked or even introduced orally to human body [16]. The detailed mechanisms of its effect have not been fully understood yet. Therefore, different studies were conducted to reveal

these mechanisms and to allocate biomarkers for their possible determination [17]. It is worth noting that some medications used for mitigating symptoms of Parkinson's disease, like selegiline (SE), can produce *l*-MAPA as a metabolite upon ingestion. Shin et al. [18] studied this phenomenon in urine samples and confirmed the observation by using headspace–solid phase microextraction (HS-SPME) coupled with gas chromatography–mass spectrometry (GC-MS). Undoubtedly, this metabolite should be distinguished from people who consume MAPA illegally.

Sensors are among the analytical methods utilized for detecting MAPA in bio and non-bio samples. They have been used in various fields, including environmental analysis [19-20], forensic studies, and drug identification and quantification [21]. They are miniature analytical devices that can determine the presence of analyte species and measure their concentration in different media. There are various types of chemical sensors, including optical, magnetic, thermal, and electrochemical sensors. They differ in the working mechanisms and the type of measured signals. Sensors consist mainly of a recognition element, a transduction element, and a signal processor for recording the chemical concentration. Different sensors have been proposed and used for MAPA quantification with high selectivity and sensitivity. The improvements in validation parameters have been achieved by modifying biological receptors, such as antibodies [22], DNA, and enzymes, or by using nano-based materials to modify electrode surfaces [23].

As sensors are instrumental methods, constructing calibration curves is necessary to study the relationship between different concentrations of MAPA and the physical properties measured by the sensors. From the calibration curve, different validation parameters can be extracted, such as the method linearity range, limit of detection (LOD) and limit of quantification (LOQ). The way to enhance these validation parameters is by improving the response of the instruments or sensors. This could be achieved by better engineering the sensing electrodes, which can be enhanced by modifying their components, specifically, the materials employed for constructing the sensing electrodes in sensors. When excavating the MAPA world, MAPA impacts geographical boundaries and influences the communities worldwide. Thus, sensor scientists have published tremendous work worldwide focusing on finding a reliable, fast method for its on-site MAPA determination in various samples. This paper aims to review the optical and electrochemical sensors that have been employed for the detection of MAPA since 2012.

■ REPORTED SAMPLE PREPARATION METHODS

The pharmacokinetics journey of MAPA, in the human body, starts from administrating it orally by eating, smoking or injecting it into the bloodstream. After that, the MAPA metabolites, which resulted from MAPA reaction with human organs, can be excreted from human fluids, like urine, oral fluid and blood plasma (as shown in Table 1), from which the prominent MAPA-metabolite, or by-products known as amphetamine (APA), or the other metabolites like *para*-hydroxy-MAPA and *para*-hydroxylation can be detected [24-25]. The analysis of these sample types is important for forensic investigations.

It is worth noting that exposure to MAPA can be direct (for users) and indirect. The latter type relates to individuals who do not directly consume MAPA but rather obtain it from users or contaminated surfaces, such

Table 1. A summary of sample types and their advantages for MAPA analysis

Sample	Advantages	Ref.
Hair	Provide a stable and long-term record of exposure to MAPA	[26]
Vapors	Safe, non-destructive, invasive	[27]
Oral fluids	Easy sampling and non-invasive	[28]
Urine	Easy sampling, non-invasive, detection window can be days to weeks	[18]
Blood	Rich genetic molecules	[29]
Solid	Easy sampling from different sources, various compositions	[30]

as ceilings or internal parts of cars where MAPA is used [31-34]. In other words, MAPA can be synthesized in clandestine laboratories, and this, of course, has a direct negative impact on the workers or indirect harm to their families [35]. Additionally, MAPA can be transferred by hand and clothing from one area to another, making exposure to contaminated surfaces a possible source of MAPA contamination [36].

MAPA can be dissolved in some organic solvents, such as chloroform, ethyl acetate, and diethyl ether. So, it is back-extracted without loss by using an acidic medium. The possible loss may occur if the extraction procedure includes evaporation due to MAPA volatility. To overcome this, the use of hydrochloric acid or dimethylformamide can minimize or avoid the loss process [3]. As MAPA is a volatile compound, GC is mostly suitable for its analysis [37-38]. Usually, MAPA and its metabolites are present in trace amounts in human-based samples. The samples cannot be directly subjected to analytical instruments due to their complex nature. Hence, pretreatment is required for separating MAPA from the matrix. There are several factors that determine the selection of the preparation method, namely, matrix type, properties of the analyte, analyte concentration in the sample, the chosen analytical method and the analysis time.

Extraction Methods

Different techniques have been used for sample pretreatment before MAPA analysis, which depend on the various analytical methods used. These preparatory steps include extraction, preconcentration and derivatization. Reported MAPA extraction methods include electro-membrane extraction (EME), liquid-liquid extraction (LLE), liquid-liquid microextraction (LLME), dispersive liquid-liquid microextraction (DLLME), solid phase extraction (SPE), magnetic solid phase extraction (MSPE), capillary microextraction (CME), HS-SPME and liquid-phase microextraction (LPME) [39].

Among the extraction methods, EME is simple, rapid, consumes small amounts of solvents and is cost-effective. In EME, MAPA is extracted through a vacuous membrane filled with an organic solvent. It uses electrical potential to divide the donor phase (aqueous medium) from the acceptor solution (inside the vacuole membrane). Under the influence of the applied potential, charged analytes in the donor phase moved to the acceptor solution, which can then be analyzed by GC or high-performance liquid chromatography (HPLC) [38].

As for LLE or LLME, samples are collected by a fluid sampling tool, mixed with two different polarity solvents to undergo partitioning, then MAPA is transferred to one of the solvents, dried, and reconstituted by dissolving the residue in a suitable solvent or the mobile phase (if chromatographic analysis is selected) [40]. The extraction efficiency is affected by the MAPA properties (solubility and pKa), polarity of the solvent, solvent volume, number of extractions, and H_2O: solvent ratio. For example, Radwan et al. [41] studied the extraction efficiency of MAPA from human urine by using different solvents and found that using an alkaline solution with methyl *tert*-butyl ether (MTBE), then using HCl spiked with propranolol as an internal standard, for back-extracting MAPA produced the highest extraction efficiency.

Regarding SPE, two phases are involved: a solid phase and a liquid phase. SPEs are made from different polymers, having commercial names like Oasis HLB, Isolute SLE+ and Extrabond EB2 cartridges, each of which has the ability to extract different drugs at different pH values [42]. Sorbents in cartridges comprise the solid phase, while the liquid phase is made of organic solvents. Different stages are presented during SPE, such as conditioning the adsorbent, introducing the sample, the adsorbent wash, the adsorbent dry, and then eluting the analytes. Analytes are extracted with the sorbents, then eluted with the liquid solvent. Different sorbents have been employed in SPE, such as molecularly imprinted polymer (MIP) [43], nano-carbonaceous material [44-45], and magnetic nanoparticles [46-47]. Although SPE is used by various research groups, its popularity is decreasing due to some drawbacks, including the high sample volume, time consumption and unsatisfactory reduction of matrix effect [48], although loss of MAPA amounts may be encountered during the evaporation process by using 0.01% HNO_3 dissolved in methanol [49]. It is essential to select an

appropriate adsorbing material, washing and elution solvents that are suitable for MAPA, and modify the SPE components, like using 96-well plates for better extraction [50-51].

The extraction of MAPA from different samples is useful for forensic analysis. For example, a cationic exchanger of silica can be used as a sorbent in SPE for extracting MAPA from ground and river water samples. Suspended particulate can be removed from the samples by a membrane filter, then exposed to a silica exchanger, which should have been cleaned with alkaline water and placed inside the SPE, the analytes can be passed through the cartridge and eluted with a mixture of acetone and ethyl acetate. The extract should then be dried under a stream of nitrogen and reconstituted with 500 μL of the mobile phase before chromatographic analysis [52]. It was found that the selectivity of separating MAPA and muscimol would be enhanced when an adsorbent is bonded with a single molecule having double opposite charges. This occurred during the interaction between the drugs and the double-zwitterionic SP, as observed using liquid chromatography [53].

Hair can be used in forensic detection because it is easy to sample, has high stability and can contain drugs for months after consumption. SPE can be utilized to extract MAPA from hair prior to chromatographic analysis [26]. After collecting hair, it should be acetone-washed, powdered, soaked in HCl solution at 53 °C for overnight then extracted by SPE. Marfey's reagent can be used to derivatize the extract before the chromatographic analysis. MAPA may be present in urine; using traditional SPE is challenging. To improve its extraction, graphene oxide (GO) substrates coated with different nano-adsorbents like polyaniline or Fe_3O_4/C-nanodots are advisable prior to using the LC method [54]. Dispersing carbon nanodots through the carbon layers would overcome the closure of the active adsorption sites in GO that results from the stacking of carbon layers.

MSPE, involving Fe_2O_3, uses acid-oxidized multiwalled carbon nanotubes (MWCNTs) to extract MAPA and ketamine from biological samples. High affinity of the drugs towards MWCNTs is observed. This is due to bi-bi stacking interaction derived from the aromatic rings, also the functional groups of the drug's surfaces provide good chelating sites [55]. The magnetic adsorbent can be further improved by carbon coating [56]. Furthermore, the combination of MSPE and bio-DLLME can enhance the extraction and pre-concentration of MAPA in human urine samples. The use of methanol and rhamnolipid biosurfactant as a binary part enables the extraction of MAPA. This binary part has several advantages, such as decreasing the interfacial tension and being environmentally friendly [57]. Moreover, the MSPE can be improved by coating magnetic nanoparticles with poly(3-thienylboronic acid. This enables MAPA extraction from human urine [46]. Additionally, the use of a nanocomposite of GO and Fe_2O_3 would further enhance the extraction from human urine [58]. The same nanocomposite is applicable for fast extraction of MAPA from supplements of sports and weight control within 3 min. Simply, the sample solution should be treated with tiny amounts of GO and Fe_2O_3, then shaken for MAPA extraction [47].

As each extraction method has its advantages over the other methods, combining different extraction methods shows improvements in the preconcentration process. For instance, combining LLE and DLLME for improving MAPA extraction from human urine. Urine and CH_3CN can be mixed and passed through a column filled with NaCl to form CH_3CN droplets in a salting-out effect. The droplets can then be extracted using a syringe and mixed with 1-undecanol. The mixture should be treated with K_2CO_3, then used in DLLME. The combined extraction techniques can provide MAPA recoveries up to 108% [59]. Further improvement in the extraction requires using ionic liquids like 1-butyl-3-methylimidazolium bis (trifluoromethyl) imide, which have been utilized for extracting MAPA [60]. Also, the usage of a combined ionic liquid, 1-octyl-3-methylimidazolium hexafluorophosphate, and CH_3OH during the extraction from human urine, to eliminate health and environmentally related issues, results in recoveries over 80% [61].

As the usage of LLE and SPE has some drawbacks, such as analyte loss, consuming large solvent volumes and having relatively low precision, SPME can overcome

these limitations. It also presents useful applications for the extraction of volatile compounds from biofluid specimens. For example, the use of different polymeric fibers, like dodecyl sulfate-doped poly-pyrrole (PPy-DS), makes it suitable for a variety of biological samples [62]. As the fibers are non-polar, SPME is primarily used in conjunction with GC. Derivatizing the analyte or modifying SPME can enhance selectivity and sensitivity. In one of the studies, MAPA was dissolved in acetonitrile and injected via a syringe into a designed unit for making MAPA vapors. These vapors can be sampled by SPME, which has poly(dimethylsiloxane) (PDMS), before using GC-MS [27]. Another modification can be attained by attaching the holder of the SPME fiber to a stainless-steel tube, then coupling it to an air sampling pump. This adaptation has been proven successful in collecting MAPA vapors from clandestine laboratories; the vapors can then be analyzed by GC-MS. This method is suitable for sampling MAPA indoors, breath, vehicles and containers as no expensive tools were used, and the sampling time was short [63].

Regarding CME, the work conducted by Nair and Miskelly [64] illustrated the use of CME for extracting MAPA vapors produced by a vapor dosing system. MAPA vapors in clandestine laboratories were collected onto glass filters that were coated with PDMS coating. It was claimed that the sensitivity of CME is better than SPME under the same sampling conditions. Later one, pentafluorobenzyl chloroformate was loaded before sampling to conserve the MAPA concentration for five days after sampling. Although the sensitivity of this method exceeded SPME by 60 times, it is not used for outdoor sampling yet [65].

Derivatization Methods

Several chemicals have been used to derivatize MAPA for enhancing its qualitative and quantitative analysis. For example, a composite having 1,2-naphthoquinone-4-sulfonate and polydimethylsiloxane/tetraethylorthosilicate/SiO_2 NPs, was used to derivatize MAPA prior to spectroscopic measurements [30]. Also, MAPA in different urine samples was individually derivatized by heptafluorobutyric anhydride, pentafluoropropionic anhydride, trifluoroacetic anhydride, acetic anhydride and *N*-methyl-bis(trifluoroacetamide), before GC analysis [66-67]. Also, extracts having MAPA may be evaporated, then treated with trifluoroacetic anhydride alone [43], pentafluoropropionic anhydride [68], trifluoroacetic anhydride in ethyl-acetate [69], pentafluorobenzyl chloroformate or L-*N*-(trifluoroacetyl)prolyl chloride for derivatizing MAPA before GC-MS measurements [65,70]. Also, oxidation and silylation can be used for derivatization [71]. It is important to mention that the derivatization of MAPA is not usually required when using HPLC, unless for the separation of MAPA enantiomers by using HPLC-tandem MS, which may require the derivatization of MAPA to reduce the analysis cost, by eliminating the use of chiral columns.

■ DETECTION METHODS

The scientific publications worldwide have shown huge amounts of work, based on using analytical methods that determine MAPA and its metabolites in various samples. Some scholars claimed the ability to determine MAPA in seized samples by using the chloride test [72]. The current work focuses on the use of sensors for the detection of MAPA. Their working mechanism would be briefly explained besides the validation parameters like the method linearity range, LOD and LOQ.

Sensors

Sensors are relatively simple, easy, and consume relatively small amounts of reagents when compared to other analytical methods. Sensors are made of two preeminent components: the recognition material and the transducer. Analytes can bind to the recognition elements in biological receptors, part of biosensors. Sensors found applications in drug detection in various sample types. The selection of a suitable sensor for certain analysis is influenced by some factors, such as selectivity (the prime importance), sensitivity level and the matrix nature [73]. Different approaches can be followed to achieve excellent selectivity; the sensor must be able to discriminate between the analyte and other chemicals present in the matrix. Also, the selectivity can be enhanced by integrating MIP, or molecular

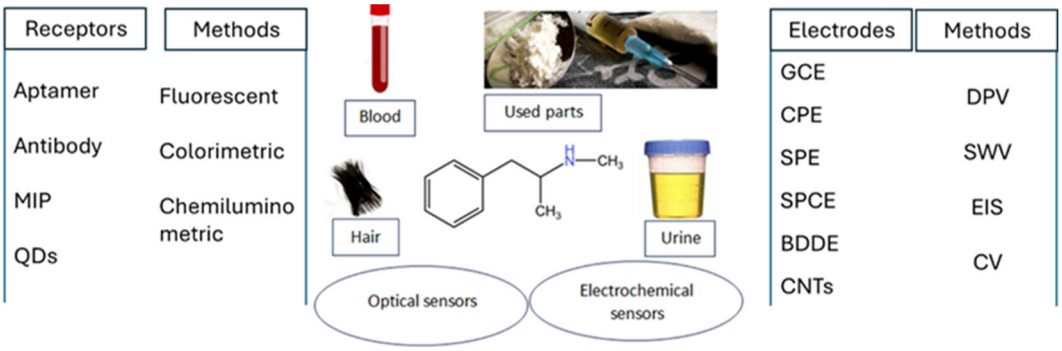
recognition elements, like aptamer, which is derived from DNA, that would create a signal upon binding with the analytes [74-75].

Moreover, the use of nanomaterials would improve the selectivity and sensitivity of the biosensors [76]. Sensors can be fabricated onto paper or flexible substrates at a small scale, which makes them favorable for an in-field detection process. In one of the studies, the concentrations of different drugs are determined by using colorimetric sensor fabricated onto test paper. The produced color's shade was processed by a digital camera, which facilitates its on-site analysis [30].

Nowadays, smartphones are equipped with large computing power and are capable of assisting the on-site drug detection applications. In this instance, Krauss et al. [77] introduced a fascinating method to detect some illegal drugs onsite. Their idea used smartphones to identify the color changes of images taken during the detection process, for defining the threshold values of different chemicals like MAPA. Although Guo et al. [78] fabricated smartphone-based fluorescent sensors that relay on antibody-antigen binding for ketamine fluorescence, Fan et al. [79] designed a dyed nanobead matrix with oil-soluble dyes, widely applied to prepare NPs-based lateral flow immunoassay strips that enable the MAPA sensing with naked eyes, and obtained LOD of 8 μg/L. As various examples of using sensors for detecting MAPA have been reported in the literature, they can be simply divided into optical and electrochemical sensors, as shown in Scheme 1. Optically, they can be fluorometric, colorimetric, or chemiluminometric sensors. Electrochemically, MAPA was detected by using many electroanalytical methods based on voltammetry and its derivatives, as illustrated in Table 2 and 3.

Optical sensors

Optical sensors operate by measuring the changes in



Scheme 1. Illustration of some optical and electrochemical sensors' methods and materials used for methamphetamine detection

Table 2. A survey of some optical sensors employed for the determination of methamphetamine

Detection method	Electrode	Sample	Linear range (μg/L)	Detection limit (μg/L)	Ref.
Fluorimetry	SiO_2@CQDs@mesoporous-MIPs	Human urine and blood	746–37.31×10³	238	[90]
Fluorimetry	Aptasensor	Human blood	0.746–23	149	[92]
Fluorimetry	Modified aptasensor	Human blood plasma and urine	$1.99 \pm 0.37 \times 10^{-2}$ –18.5 ± 1.0	$6.02 \pm 0.15 \times 10^{-3}$	[96]
Colorimetry	Modified aptasensor	Human urine	$298–1.49 \times 10^3$	122	[102]
Colorimetry	Modified aptasensor	Human urine	0.07–29	0.014	[103]
Colorimetry			0– 0×10^3 (MOR)	0.21×10^3 (MOR)	[106]
			$0–100 \times 10^3$ (MAPA)	0.49×10^3 (MAPA)	
Chemiluminescence	NR	Human urine	6.7–400 (FLS)	86×10^{-3} (CLS)	[110]
			25×10^{-2}–125 (CLS)		

optical features, like absorbance or fluorescence, that result from biochemical light-MAPA interaction, like colorimetric and fluorescence changes, to detect MAPA presence. In another words, the light absorption is measured by UV-vis spectrophotometry, whereas the emitted light after excitation is measured by fluorescence spectroscopy. These sensors can produce non-invasive, rapid and highly sensitive analysis. Molecular probes used in different optical sensors have distinguishing optical interactions upon contacting MAPA, making real-time qualitative and quantitative investigations possible.

Fluorometric sensors (FLS). These sensors used some organic derivatives as fluorescent probes, which emit fluorescence proportional to the MAPA concentration when exposed to UV light. The probes can be pristine or doped organic fluorescent materials, naphthalimide-based materials, quantum dots (QDs), or MIP, for detecting MAPA in different types of samples [80-92]. He et al. [80] proposed the first fluorometric sensor for detecting MAPA by using polyfluorenes. The utilization of the amine side of a polyfluorene as the fluorescent (FL) probe that was quenched upon interaction with MAPA, produced LOD of 26.6 μg/L. Another polymers, named as (poly[(9,9-dioctylfluorenyl-2,7-diyl)-*alt*-(2,1,3-benzothiadiazole-4,7-diyl)]), (poly[(9,9-dioctylfluorenyl-2,7-diyl)-*alt*-(2,1,3-benzooxadiazole-4,7-diyl)]) and (poly[(9,9-dioctylfluorenyl-2,7-diyl)-*alt*-(quinoxaline-5,8-diyl)]) and denoted as P1, P2 and P3, respectively, were used for studying MAPA vapors. The highest selectivity and sensitivity were observed when using P1 polymer, yielding 191 μg/L as LOD [81].

Another fluorescent probe used for MAPA sensing is based on naphthalimide. The sensing is improved by doping it with silica nanoparticles (SiO_2 NPs) [82]. The thiophene part of the sensor binds to the amine part of MAPA, lowering the effect of internal heavy atom and improving the FL signal. This was confirmed in a linear concentration range of 0.99×10^3–40.29×10^3 μg/L. Fluorescent sensors can also detect MAPA that is presented as vapors in the air, which facilitates non-invasive detection. Supporting this, work reported by Li et al. [93] and Liu et al. [94]. In Li et al. work, a fluorescent polymer probe is attached to a UV-ozone treated substrate, which enables the detection of methylphenethylamine with LOD of 25×10^{-2} μg/L [93]. Liu et al. utilize perylene bisimide derivatives for fluorescent sensing of many illicit drugs. Although the MAPA vapors have been diluted thousand times by the air, the sensor could still detect MAPA presence with little effect from the odorous substances [94]. Unlike the previous approach, Zhang et al. [95] followed a chemical approach for constructing a sensor based on conductivity. MAPA was detected by carbon nanotubes-functionalized poly[3-(6-carboxyhexyl)thiophene-2,5-diyl)], which is sensitive to amine vapors, with a LOD of 4 μg/L.

Owing to the viable properties of QDs, such as narrow emission, broad absorption wavelengths and biocompatibility [83-85], MAPA has been sensed by a bioreceptor that is based on CdS QDs. An antibody of MAPA was immobilized onto a platform of CdS QDs as the receptor. The QDs were capped with mercapto-acetic acid by using the coupling agents (*N*-ethyl-N_0-(3-dimethylaminopropyl carbodiimide) and sulfo-*N*-hydroxysuccinimide. The improved immunosensor had high selectivity, even in the presence of other drugs, and sensed MAPA with a LOD of 118 μg/L [86]. Another example of QDs is graphene QDs, which have remarkable optical features and biocompatibility [84]. Following a similar approach, carbon QDs were immobilized onto SiO_2 to fabricate a fluorescent probe for detecting MAPA [90]. Also, CdTe QDs find applications in biosensors for MAPA detection with LOD down to $60.20 \pm 1.56 \times 10^{-4}$ μg/L [96].

Although the immunosensors showed remarkable advantages, they suffer from some drawbacks regarding cost and durability. Hence, other receptors like MIP have been proposed as alternative binding sites templates due to their lower cost, ease of fabrication, high selectivity and being reusable [88]. In addition, MIP has been combined with graphene QDs to add their advantages in terms of the enhanced surface area and the conductivity. This combination is used to amplify the MAPA sensing signal. The composite structure showed high selectivity towards MAPA, as MAPA was able to quench the FL signal, whereas other presented drugs could not. MAPA was detected as low as 1.7 μg/L [89].

This approach is suitable for the detection of MAPA in blood serum or plasma, as it can overcome the blood matrix effect that results from MAPA interaction with blood chemicals. Another approach has been reported by Goulding et al. [91] who introduced a complex of nano-MIP beacons/aptamer for detecting MAPA in human urine and serum samples. The use of these beacons has shown remarkable quenching for MAPA that improved MAPA detection among other drugs presented in forensic samples [91]. Another solution to overcome the limitations of immunosensors is by adopting a single strand of DNA or RNA, known as an aptamer, which has high selectivity towards the targeted analyte. The biosensor found applications in determining MAPA, carbon QDs were fabricated as donors, whereas cobalt oxyhydroxide was used as an acceptor. The fluorescence of carbon dots was quenched upon interaction between the donor and acceptor [92].

Furthermore, a non-invasive optical sensor for detecting MAPA and cocaine by using rhodamine B-labelled polymer bodies was developed by Ghorbanizamani et al. [97] and reported LOD of 0.37 and 0.49 ng/mL for MAPA and cocaine, respectively from saliva samples. The search for rapid fluorescent sensing of MAPA with recoveries above 94% has recently been reported by Awata et al. [98]. MAPA has been sensed according to the host-guest molecular interaction. The utilization of cucurbit[7]uril (CB[7]) as a host molecule that encapsulates acridine orange (AO), an indicator fluorescent dye, as a guest molecule. The signal of AO is shifted upon sensing MAPA, and MAPA can be detected by the naked eye down to 2.98 μg/L.

Colorimetric sensors (CS). In colorimetry, the compounds of interest are made colorful by using specific reagents to detect them easily. Colorimetric sensors are simple, cost-effective and use a spectrometer for measurements [99]. However, the reliability of these sensors may be affected by contamination and interference from the matrices. Their performance can be advanced by following some promising strategies. One of which is by employing nanomaterials like metal NPs, as the manipulation of the NPs' size can alter the optical properties. The surface plasmon band can be shifted by altering the interparticle plasmon coupling. The dispersion and aggregation of NPs influence the NPs' color [100]. Another strategy is to use a composite of 1,2-naphthoquinone-4-sulfonate and polydimethylsiloxane/tetraethylorthosilicate/SiO_2 NPs for derivatizing MAPA; which would color MAPA to assist its spectrophotometric determination in street samples. The fabricated device recognized the analytes in street samples with a LOD of 964.1–2411.7 g/L [30]. Additionally, Yarbakht and colleagues [101] introduced the first aptamer-based sensor for detecting MAPA. The use of DNA nucleic acid aptamer decorated with gold NPs for colorimetric sensing enhanced the MAPA detection as the aptamer structure changes in the presence or absence of MAPA. It was appealing for detecting MAPA at concentrations as low as the μM range. Nevertheless, the use of aptamer linked to unmodified fold NPs for MAPA sensing is possible, as the aggregation of the unmodified NPs induced by salt could change the solution's color from red to blue, which indicates the presence of MAPA [102].

The response of aptamer can also be enhanced by gold@silver NPs, a combination of GO, cetyltrimethylammonium bromide (CTAB) gold NPs, especially when other drugs like cocaine are presented in the sample [103-105]. Magnetic beads (MBs) are combined with an aptasensor and NPs for detecting MAPA and cocaine simultaneously. Gold@silver (Au@Ag) NPs core shells were coated with a single-stranded DNA as an aptamer. The absence of the analytes did not cause a color change; however, their presence created a competition for the aptamer to bind with the analytes and emit a color accordingly [103]. In another strategy, MAPA and cocaine have been simultaneously detected in spiked wastewater. Reporter probes (RPs) are fabricated by functionalizing the synthesized Au NPs and Au@Ag NPs with DNA. The two drugs have been detected by two capture probes (CPs) that were coupled with MBs. The two drugs underwent DNA-DNA hybridization with individual RP and CP in a folded structure, which then unfolded by applying an external magnetic field. The presence of each drug that has a high affinity towards the aptamer

could dismantle the structure and change the supernatant color. The color change increases linearly with increasing MAPA concentrations in the range 0.07–29.84 μg/L [104]. Bastami et al. [106] showed that the addition of small amounts of Cu during the ultrasonic irradiation for the synthesis of Ag NPs improved the sensor's sensitivity towards MAPA and morphine (MOR) during the analysis of street samples. In another strategy based on improving the aptamer-based colorimetric sensors, Adegoke et al. [105] reported the development of a DNA aptamer, the bioreceptor, by multi-shaped GO cetyltrimethylammonium bromide (CTAB)-AuNPs hybrid nanozyme. The catalytic signal can be amplified by hemin.

Chemiluminometric sensors (CLS). CLS functions by transforming a chemical reaction's energy into light, which can then be detected and measured to quantify MAPA. The gist base involves the formation of high-energy intermediates that liberate photons as they revert to the initial stable state. The CLS outperforms the CS and FLS in having low background interferences [107-108]. MAPA interacts with the blood matrix in blood serum and plasma, hence influencing analysis signals; mitigating these interferences is vital for the analysis. One of the studies, reported the development of a portable chemiluminescent fiber-based sensor to enhance MAPA sensing in different human-based fluids, with a linear response range of 0.001–0.3 μg/mL with LOD to 5×10^{-4} μg/mL [109].

A combination of CTAB, rhodamine B (R-B), L-cysteine capped with QDs of CdS was used for fabricating a sensor established on FL and CL methods. The intensities of emission of both CL and FL, which resulted from the reaction between MAPA and RhoB-CTAB-$KMnO_4$, were monitored by the change in the emission intensities of CdS QDs. The CL emission and FL emission of CdS CQs were linear over 26.56–133 and 7.16–425 μg/L, respectively [110].

Although optical sensors are non-invasive, have high sensitivity, and can detect low MAPA concentration, several difficulties remain. They are affected by complex sample matrices and need frequent calibrations. Moreover, delicate instrumentation is required for their operation, which requires cost consideration when utilizing these methods. Additionally, controlled conditions are crucial when utilizing these sensors for outdoor applications, as ambient light interference can be a significant issue. More work on coupling optical sensors with scanners that operate on smartphones is necessary, so that quantitative analysis can be performed outdoors accurately. Furthermore, there is still a need to develop near-infrared fluorescence probes, that enable the reduction of possible matrix interference in complicated samples, which would enhance the implementation of this technology.

Electrochemical sensors

The detection of MAPA by electrochemical sensors is mainly based on voltammetry-derived techniques. In voltammetry, a working electrode is subjected to a single or varied potential. This potential is to oxidize or reduce the analyte species, which can be visualized on a voltammogram. The electrochemical measurements are made in certain media that have electrolyte support. The choice of the used media is affected by some physical properties of the targeted drugs. The sensing property in this type of sensor is affected by the immobilization of the receptors onto the electrode surface. This is because MAPA would be attracted to the electrode surface hence electrode interface engineering is of prime importance. The modification in materials is substantial for enhancing sensor performance. Materials like MIP, aptamer and antibodies can sense the MAPA and they should be stable onto the surfaces of sensing electrodes [111-114]. MAPA has been sensed by various modified and unmodified electrodes, such as glassy carbon electrode (GCE), carbon paste electrode (CPE), screen-printed electrode (SPE), screen-printed carbon electrode (SPCE), boron-doped diamond electrode (BDDE), carbon nanotubes (CNTs), pencil graphite electrode (PGE), gold disk electrode (GDE) and wood-derived ionic conductive cellulose. Samples of using these electrodes and electroanalytical methods are presented in Table 3.

As already mentioned, MAPA can be detected by various electroanalytical sensors. These are voltametric, potentiometric, amperometric and impedimetric sensors.

Table 3. A survey of some electroanalytical techniques employed for the determination of methamphetamine

Detection method	Electrode	Sample	Linear range (μg/L)	LOD (μg/L)	Ref.
DPV	BDDE	Human urine and serum	$10–11.93 \times 10^3$	7	[118]
DPV	PGE	Human urine and blood	$11–8.06 \times 10^3$	7	[119]
DPV	Modified GCE	Human saliva, urine and blood	$10.64 \times 10^6–106.42 \times 10^6$	13.91×10^3	[122]
FFT-SWV	Modified CPE	Human urine and serum	$1.49–14.92 \times 10^3$	0.12	[88]
SWV	Modified GCE	Human urine	$7.46–7.46 \times 10^3$	2.38	[127]
SWV	Modified GCE	Human plasma	$3.73 \times 10^3–24.77 \times 10^3$	1.29×10^3	[128]
SWV	Modified GCE	Human urine and blood	$0.746–29.85 \times 10^3$	0.1	[129]
Amperometry	Modified gold electrode	Spiked bovine serum	$1.49–0.74 \times 10^3$	1.12	[142]
SWSV	Modified SPE	NR	2.98–14.9 and $0.44 \times 10^3–7.46 \times 10^3$	0.895	[149]
EIS	Modified SPE	NR	1.72–4.01	4.48×10^{-2}	[149]
EIS	Modified GCE	Spiked urine samples	$7.46 \times 10^{-2}–40$	2.39×10^{-2}	[147]
Electrochemical	Modified aptamer sensor	Human urine and blood	$1.49 \times 10^{-4}–10$	2.54×10^{-6}	[133]
Electrochemical	Modified graphene electrode	Saliva and household surfaces	$0.14 \times 10^3–4.48 \times 10^3$	40	[138]
DPV	Gold SPE	Human saliva	5–1000	0.56	[125]
SWV	Graphite SPE	On-site analysis of cargos	$7.46 \times 10^3–373 \times 10^3$	2.49×10^3	[151]
DPV	Modified gold electrode	Spiked urine	0.1–50	467×10^{-3}	[22]
DPV	Modified GCE	Household surfaces	$0.14 \times 10^3–5.96 \times 10^3$ and $5.96 \times 10^3–17.91 \times 10^3$	50	[131]
DPV	Modified GCE	Human urine and blood	14.77–1120 and 1120–8940	4.48	[148]
Electrochemical	Glove substrate modified with Ag nanoparticles	Spiked beverages	$0.01 \times 10^3–5 \times 10^3$	0.1×10^3	[135]
Electrochemical	Paper substrate modified with Ag and ZnO nanocomposite	Spiked beverages	$0.01 \times 10^3–6 \times 10^3$	0.1×10^3	[136]
CV and EIS	GCE modified with	Spiked urine	0.074–74.62	1.5×10^{-4}	[132]
AdSDPV	3D-printed graphite/polylactic acid electrode	Forensic samples	149.24–11.19	14.92	[150]
CV	Modified GCE	Human hair and urine	$1.49 \times 10^2–5.22 \times 10^2$	5.22	[134]

The voltametric sensors operate by cyclic voltammetry (CV) [115-117], differential pulse voltammetry (DPV) [118-119], square wave voltammetry (SWV) [120], Fourier-transform square-wave voltammetry (FFT-SWV) [89,121], square wave stripping voltammetry (SWSV) techniques. CV is a simple electrochemical technique that is usually used for studying oxidation-reduction reactions and kinetic parameters of the analytes' sensing electrodes. Although CV provides useful information regarding redox reactions, it is not as sensitive as other electroanalytical methods [115-116]. Au NPs and chitosan were blended together to form a nanocomposite for an aptasensor, which is used for detecting MAPA. The use of NPs improved the chitosan stability. The CV measurements determined MAPA, where the peak current of the electrochemical probe, ferro/ferricyanide, changed, indicating the capability to determine MAPA with a LOD of 1.49 μg/L [117]. Compared to CV, DPV is more sensitive due to lowered background current as the sensing current is measured at each applied pulse. DPV is derived from staircase voltammetry or linear sweep voltammetry. In DPV, a series of voltage pulses is superimposed onto increased potential of stairsteps or linear sweep voltage, then the produced current is measured just after or before every pulse. The literature witnessed the use of DPV more than the other electrochemical methods.

BDDE has been employed for studying MAPA in basic medium of Britton-Robinson buffer (BRB) in which the MAPA oxidation peak, by DPV measurement, was observed at 1.23×10^3 mV against silver/silver chloride (Ag/AgCl) reference electrode. The MAPA oxidation mechanism has been proposed as 2 protons/2 electrons [118]. Another electroanalytical sensor based

on PGE was fabricated by Oghli et al. [119]. The presence of oxygen in the functional groups can improve the PGE surface and enhance the electrochemical activity of PGE, as proven by DPV measurements, which enables MAPA to be detected in human-based samples at very low concentrations.

Whilst MIPs emulate natural receptors to extract MAPA from different specimens more actively, at nanoscale modifications, like SPCEs, raise the electron transfer kinetics for MAPA sensing. Upon combining with bio-recognition compounds, for example, artificial antibodies and aptamers, these substances make the use of proper molecular targeting probable, even in tricky admixtures, as in saliva and wastewater. Additionally, portable systems accentuate the relationship between nanotechnology and microfluidics. Due to its advantages over GCE and PGE, like larger surface area and µL solution capacity, SPCE, as a sensing electrode, and *N,N0*-(1,4-phenylene)-dibenzenesulfonamide, as an intermediate for detecting MAPA in human saliva. The determination process is run by SWV. The SWV measurement detected MAPA within 60 s and had a LOD of 192 µg/L [120].

The modification of CPE with MIP/multi-walled (MW) CNTs composite was used for detecting MAPA. The FFT-SWV measurement showed an oxidation of the secondary amine of MAPA at 1 V. The sensor displayed large resistance to interference during π-π stacking interactions between the molecules of interest and the template molecules. The method showed a linear response for concentrations of $1.49–14.92 \times 10^3$ µg/L [89]. This performance is due to remarkable properties of CNTs, such as large surface-to-volume ratio, high durability under thermal and chemical conditions and high electron transfer [121].

GCEs have been used as sensor platforms for detecting MAPA. Several modifying agents have been employed to improve GCE performance, such as immobilizing antibodies onto GCE that had been modified by a fluorescent-labeled polypeptide. This sensor showed application in determining MAPA in spiked human samples, and its performance was studied by DPV. The modification enabled the detection of MAPA as low as 13.91×10^3 µg/L [122]. Another modification was applied by using Nafion-$[Ru(bpy)_3]^{2+}$ for detecting MAPA in oral fluids. The obtained LOD was 10 µM [123], whereas LOD of 2.98 µg/L was obtained by Xie et al. [124], and even lower LOD down to 72×10^{-2} µg/L was achieved [125]. Conversely, the use of optical sensors for detecting MAPA produced low LODs like 9.7 µg/L [126], and 50×10^{-2} µg/L [109].

Moreover, the weak oxidation ability of bare GCE can be overcome by modifying its surface to improve its catalytic activity [127-129]. For example, by using a combination of MWCNTs amine-functionalized decorated with Au NPs and SiO_2@Fe_3O_4 [127]. Electron transfer between MAPA and MWCNTs can be assisted using SiO_2@Fe_3O_4. The SWV measurements have shown the electrochemical mechanism to be controlled by diffusion. Another strategy uses reduced GO (rGO) decorated with CeO_2 NPs for modifying GCE. The sensor screened MAPA with minimized overpotential and had a good peak current when compared to bare GCE. The oxidation process of MAPA was proposed to be 2 electrons/2 protons [124]. Furthermore, Riahifar et al. [129] modified GCE by incorporating a Fe_3O_4@poly pyrrole core-shell and rGO, then used it to detect MAPA in urine and blood samples in a slightly basic medium of Britton-Robinson buffer solution.

It has been proven that modified electrodes have improved sensitivity and stability over unmodified ones when used for analyzing street samples. In one of the novel approaches, a 3-sensor array made of different carbon-based SPEs, modified with MWCNTs, graphite and graphene, was employed for qualitative analysis of MAPA and other illicit drugs [130]. The SWV analysis for each modified electrode produces a single oxidation peak, used for the qualitative analysis of the drugs. Specifically, MAPA exhibited oxidation peaks at 700, 900, and 650 mV when using electrodes modified with MWCNTs, graphite, and graphene, respectively, against a pseudo-Ag reference electrode.

Also, modified GCEs electrodes by different carbon-based materials like GO electrodes were applied for sensing residual MAPA contamination on different household surfaces, like glass, wood, and plastic [131].

The electroanalytical analysis by DPV showed LOD of 45 μg/L. Although modifying GCE with GO reduced the peak current, due to the repulsion between negatively-charged GO sheets and the redox solution, decorating GO with Au NPs can assist in transferring electrons between the electrode surface and the redox solution, which enhanced the peak current [132]. This type of sensor conserve 90% recovery of its response after being stored at 4 °C for 30 days.

The use of aptamers as recognition units, whether pristine or doped, in biosensors for binding target molecules is widely reported. A study claimed the ability to detect MAPA by using aptamer sensor without exogenous reagents. The aptamer sequence was truncated to be in unfolded state. A conformation change occurred upon binding MAPA on the aptamer which lowered the electrical signal. MAPA was detected in different biofluids, and the method had LOD of 7.46 μg/L of MAPA in urine sample [124]. The signal of the aptamer sensor can be amplified by atom transfer radical polymerization. For instance, the sensing electrode that was already coated with azide-modified DNA and MAPA aptamer, detected MAPA in urine and blood samples. The method showed linearity in the concentration ranges of 0.149×10^{-3}–14 μg/L with 2.54×10^{-6} μg/L as LOD [133].

The polymerization of amino acids, like polyarginine, can improve the electrocatalytic performance of electrodes used in electrochemical sensors. Duan et al. [134] electropolymerized L-polyarginine to form a polyarginine membrane onto GCE. This increased the reaction sites for MAPA and improved the electrode's selectivity towards MAPA in human hair and urine samples. The sensor showed a linear response to MAPA in concentrations of 14.9–5.22×10^{3} μg/L with LOD of 4.92 μg/L.

The search for relatively inexpensive, flexible, and biodegradable substrates is essential for daily routine, to replace the glass-based sensors. To achieve these goals, extensive work has been dedicated to fabricating paper-based sensors (PBS). The combination of a flexible substrate and conductive Ag NPs has attracted the attention of researchers, such as Anzar et al. [135], for fabricating a wearable glove-based sensor for on-site use. Latex gloves can be printed with methyl aptamers then immobilized onto Ag NPs modified electrode. The effect of changing the operation temperature on the sensor performance showed 30 °C as the optimal, as beyond that temperature, the performance decreases, which may hinder its use in very hot areas. Furthermore, paper electrodes have been decorated with Ag and ZnO nanocomposite [136]. The nanocomposite can assist MAPA's binding aptamer with a sequence of ACG GTT GCA AGT GGG ACT CTG GTA GGC TGG GTT AAT TTG G, which was attached to the electrode surface. The sensor, MAPA/Aptamer/Ag-ZnO nanocomposite/paper-based substrate, showed optimal current response at 35 °C. Additionally, Suleman and colleagues [137] proposed an innovative process employing a paper-based multiple analytical device (ePMAD) platform for quick and on-site detection of MAPA and other drugs in beverages and non-alcoholic beverages. This platform incorporates Ag NPs and drug-specific aptamers. The approach is fast and detects the drugs within 30 s. Moreover, a graphene electrode was used for MAPA determination in human saliva and in household surfaces. The graphene electrode was induced by a CO_2 laser, in which a laminating film of polyethylene terephthalate (PET) was used for extracting carbon from Kapton tape. The fabricated modified graphene electrode was used for detecting MAPA in a portable sensor [138]. Interestingly, the covert sensing of MAPA is made possible by Zhao et al. [139]. The sensor was fabricated on a flexible In:SnO_2 plastic substrate as the sensing platform and utilized wood-derived ionic conductive cellulose as the conducting layer. The electrode performance improved upon adding Cu^{2+} ions.

Potentiometric and amperometric sensors. As for potentiometric sensors, there is no flow of electrical current, and the working mechanism is affected by the electrode potential. Upon immersing indicator electrodes, like ion-selective electrodes (ISEs), and reference electrodes in an analyte solution, the concentration of the ions that are present in a solution is determined by the potential difference that exists between the two electrodes, so the potential difference is

proportional to the analyte concentration. The ISEs have a selective membrane which includes an ionophore for sensing ions of interest, a plasticizer and poly(vinyl chloride) (PVC). The modification of the ISEs components would improve analytical performance. There is no study, up to our knowledge, published in the last 13 years regarding this type of sensor, although it is a simple method and does not demand tricky sample preparation. A relatively old demonstration of this sensor for detecting MAPA dates back to 1993. In that work, PVC electrode was modified with an ion exchanger, sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate. The potentiometric study conducted on human urine showed MAPA's LOD of 1.492×10^3 μg/L [140].

Unlike potentiometric sensors, amperometric sensors operate at zero voltage, while electrochemical reactions produce an electrical current. Thus, amperometry detects ions in solutions by measuring the electrical current or the changes in the electrical current. Amperometric sensors have high sensitivity over a wider linearity of concentration ranges [141]. There are limited publications associated with amperometric sensors for MAPA detection. Back to 2014, Au electrodes were modified by several components in the order of L-cystine (LC), Prussian blue (PB), nano-Au and (3-mercaptorpropyl) trimethoxysilane (MPS). The current signal was enhanced by PB as it reduced hydrogen peroxide [142].

Impedimetric sensors. Impedimetric sensors are more complicated than the already mentioned sensors, however, they can provide very useful insights regarding the characterization of the electrode double layer, the transfer of charges and the electrodes' kinetics by employing impedance spectroscopy (EIS) [143]. Yeh et al. [144] developed an impedimetric sensor for MAPA determination by constructing a bridge for the electron transfer between two electrodes. The bridge was made by coupling Au NPs with an antibody. This construction led to LOD of 100 μg/L for MAPA determination.

Au electrodes have been modified by incorporating 3-mercaptopropionic acid, as a self-assembly modifier, then activated by 1-ethyl-3-(3-dimethylaminoprophyl) carbodiimide /*n*-hydroxysulfsuccinimide. The sensor was completed by immobilizing the MAPA antibody onto the surface of a modified electrode for determining MAPA in spiked human blood [145]. Also, some Au electrodes were immobilized with different aptamer sequences through Au-thiol affinity. The composition was electrochemically evaluated by CV, DPV and EIS and the best sequence had the capability to determine MAPA as low as 467×10^{-3} μg/L [22].

The development of impedimetric sensors has been done following several approaches. For instance, adhering an aptamer onto the GCE by Au NPs, then incubating MAPA onto the surface of the aptasensor to minimize any possible interferences [146]. Also, by decorating rGO with CeO_2 NPs, it was then used to modify GCE for sensing MAPA in spiked urine samples. The aptasensor performance is evaluated by EIS measurement in the presence of ferro/ferricyanide redox probe which exhibited LOD of 0.023 μg/L [147]. Another approach is by decorating carbon nano-onions with Ag nano-dendrites then coating it onto GCE for MAPA in human urine and blood samples [148]. The use of this nano-shape of C or Ag elevates catalytic efficiency and the adhesion onto GCE surface, enabling coating of more layers, hence creating a more efficient sensing interface.

Another impedimetric sensor is made by modifying the SPE electrode with MWCNTs-nafion and Au NPs. MAPA was adsorbed onto the modified electrode, and the electrochemical study was conducted by using EIS and SWSV. The sensor exhibited LOD down to nM [149]. Treating the surface of the SPE electrode with iono-gel (a mixture of hydrogel and ionic liquid) and antibodies can improve the sensing property for determining MAPA in human saliva with a LOD of 72×10^{-2} μg/L [125]. The combination of colorimetric and electrochemical methods for detecting MAPA in forensic samples is made possible by Melo et al. [150]. MAPA is qualitatively determined by Simons's test, in which the MAPA color changes from pink to purple, followed by subsequent electrochemical confirmation. Despite having various inherent advantages, such as high specificity and sensitivity, cost-effectiveness, wide measuring range, and easy transport, are ideal for real-

time monitoring, they may suffer from interferences from complex matrices and the need for meticulous calibration of the electrodes frequently due to electrodes' fouling problems. Moreover, additional selective receptors are required for modifying the sensing electrodes to enhance specificity towards the analyte of interest. Following this, a layer of complication is added to their utility.

■ CONCLUSION AND FUTURE VIEWPOINT

For many decades, a tremendous number of articles have been published on the MAPA spread, its effect, and its determination and quantification. MAPA is adversely affecting all communities due to its easy synthesis, which makes locating its manufacturing sites difficult. Due to its presence in combination with other street drugs, its determination in various samples found interest by using different analytical methods. The current work emphasized the use of different optical and electrochemical sensors for its analysis. Although chromatographic methods have been used for MAPA analysis due to their high sensitivity, their high operation cost, required solvent volumes, training, and expensive maintenance, as well as their bulkiness, hinder their conversion into portable kits, which may not attract investment from companies. On the other hand, sensors would be suitable for the MAPA determination due to their simple fabrication, relatively lower cost, minimum solvent usage and can be easily made portable. Sensors are relatively new compared to chromatographic methods, so there is still room for improvement by manipulating the properties of the sensing electrodes through the coupling of nanomaterials with receptors, as well as by further reducing the cost of sensors through lab-on-chip technology. Additionally, the utilization of some environmentally friendly products like paper and cotton, as sorptive phases or in SPME, would conserve the environment. Usually, the probes used in optical sensors experience two issues. (1) Nearly all the probes function by the photo-induced electron transfer principle, which presents a single-signal response as fluorescence on/off. There are different non-analyte factors that would easily influence fluorescence response, which may give inaccurate and unreliable accuracy and selectivity of the determination. By means of this, other types of fluorescent probes are required. (2) Although MAPA possesses the nature of aliphatic amines and aromatic amines in its structure, it lacks the high nucleophilicity of aliphatic amines or the high energy level of aromatic amines. Therefore, it is indeed severe to erase the influence of analog amines interference. On the other hand, electrochemical sensors offer exceptional sensitivity and specificity, optimal for real-time observation and point-of-care analysis. Overall, there is still a need for developing reliable, portable, or wearable analytical devices for on-site determination of MAPA alone or in combination with other street drugs, particularly if they are presented in a liquid phase.

■ CONFLICT OF INTEREST

The authors declare that no known competing financial interests or personal relationships could have appeared to influence the work reported in this paper.

■ AUTHOR CONTRIBUTIONS

Hussain Alessa initiated the idea, collected the references and wrote the manuscript. Sulafa Jamal Mohammed Nassar revised the manuscript and drew the figures. Both authors agreed to the final version of this manuscript.

■ REFERENCES

[1] Shakeri, J., Farnia, V., Davarinejad, O., Salemi, S., Golshani, S., Rahami, B., Alikhani, M., and Hookari, S., 2020, Distress tolerance in methamphetamine and opium abusers with non-drug abuser (A comparative analysis), *Clin. Epidemiol. Global Health*, 8 (2), 513–518.

[2] Protti, M., Mandrioli, R., Gonzalez-Rodriguez, J., and Mercolini, L., 2022, Enantioselective analysis of the methamphetamine precursors ephedrine and pseudoephedrine by capillary electrokinetic chromatography using cyclodextrins as chiral selectors, *J. Chromatogr. Open*, 2, 100032.

[3] Markowitz, J.S., and Patrick, K.S., 2017, The clinical pharmacokinetics of amphetamines utilized in the treatment of attention-deficit/hyperactivity disorder, *J. Child Adolesc. Psychopharmacol.*, 27 (8), 678–689.

[4] Prakash, M.D., Tangalakis, K., Antonipillai, J., Stojanovska, L., Nurgali, K., and Apostolopoulos,

V., 2017, Methamphetamine: Effects on the brain, gut and immune system, *Pharmacol. Res*., 120, 60–67.

[5] Wearne, T.A., and Cornish, J.L., 2018, A comparison of methamphetamine-induced psychosis and schizophrenia: A review of positive, negative, and cognitive symptomatology, *Front. Psychiatry*, 9, 491.

[6] Ballester, J., Valentine, G., and Sofuoglu, M., 2017, Pharmacological treatments for methamphetamine addiction: Current status and future directions, *Expert Rev. Clin. Pharmacol.*, 10 (3), 305–314.

[7] Akhgari, M., Mobaraki, H., and Etemadi-Aleagha, A., 2017, Histopathological study of cardiac lesions in methamphetamine poisoning-related deaths, *Daru, J. Pharm. Sci.*, 25 (1), 5.

[8] Smith, L.M., Paz, M.S., LaGasse, L.L., Derauf, C., Newman, E., Shah, R., Arria, A., Huestis, M.A., Haning, W., Strauss, A., Della Grotta, S., Dansereau, L.M., Neal, C., and Lester, B.M., 2012, Maternal depression and prenatal exposure to methamphetamine: Neurodevelopmental findings from the infant development, environment, and lifestyle (ideal) study, *Depression Anxiety*, 29 (6), 515–522.

[9] United Nations Office on Drugs and Crime, 2022, *World Drug Report 2022*, United Nations, Vienna, Austria.

[10] Al-Asmari, A.I., 2021, Methamphetamine-related postmortem cases in Jeddah, Saudi Arabia, *Forensic Sci. Int.*, 321, 110746.

[11] Barnes, C., Madaras, S., Pigou, P.E., Johnston, M.R., and Kirkbride, K.P., 2019, Origins of *N*-formylmethamphetamine and *N*-acetylmethamphetamine in methamphetamine produced by the hydriodic acid and red phosphorus reduction of pseudoephedrine, *Forensic Chem.,* 13, 100158.

[12] Shekari, A., Akhgari, M., Jokar, F., and Mousavi, Z., 2016, Impurity characteristics of street methamphetamine crystals seized in Tehran, Iran, *J. Subst. Use*, 21 (5), 501–505.

[13] Biddle, T.J., Wermuth, U.D., Loughlin, W.A., Cresswell, S.L., and White, A.R., 2022, Potential forensic markers from synthetic pathways to 1-phenyl-2-propanone from uncontrolled and controlled substances, *Forensic Chem.*, 28, 100410.

[14] Toske, S.G., and McKibben, T.D., 2022, Monitoring methamphetamine in the United States: A two-decade review as seen by the DEA methamphetamine profiling program, *Drug Test. Anal.*, 14 (3), 416–426.

[15] Ciesielski, AL., Green, M.K., and Wagner, J.R., 2020, Characterization of one pot methamphetamine laboratories using GC-MS and LC-MS/MS, *Forensic Chem*., 19, 100244.

[16] Ramli, F.F., Rejeki, P.S., Ibrahim, N.I., Abdullayeva, G., and Halim, S., 2025, A mechanistic review on toxicity effects of methamphetamine, *Int. J. Med. Sci.*, 22 (3), 482–507.

[17] Wang, T., Xu, C., Xu, S., Gao, L., Blaženović, I., Ji, J., Wang, J., and Sun, X., 2021, Untargeted metabolomics analysis by gas chromatography/time-of-flight mass spectrometry of human serum from methamphetamine abusers, *Addict. Biol*., 26 (6), e13062.

[18] Shin, I., Choi, H., Kang, S., Kim, J., Park, Y., and Yang, W., 2021, Detection of l-methamphetamine and l-amphetamine as selegiline metabolites, *J. Anal. Toxicol*., 45 (1), 99–104.

[19] Pérez-Fernández, V., Mainero Rocca, L., Tomai, P., Fanali, S., and Gentili, A., 2017, Recent advancements and future trends in environmental analysis: Sample preparation, liquid chromatography and mass spectrometry, *Anal. Chim. Acta*, 983, 9–41.

[20] Kawde, A.N., Baig, N., and Sajid, M., 2016, Graphite pencil electrodes as electrochemical sensors for environmental analysis: A review of features, developments, and applications, *RSC Adv.*, 6 (94), 91325–91340.

[21] Shaw, L., and Dennany, L., 2017, Applications of electrochemical sensors: Forensic drug analysis, *Curr. Opin. Electrochem.*, 3 (1), 23–28.

[22] Bor, G., Bulut, U., Man, E., Balaban Hanoglu, S., Evran, S., and Timur, S., 2022, Synthetic antibodies for methamphetamine analysis: Design of high

affinity aptamers and their use in electrochemical biosensors, *J. Electroanal. Chem.*, 921, 116686.

[23] Khorablou, Z., Shahdost-Fard, F., and Razmi, H., 2023, High sensitive detection of methamphetamine by high-performance aptasensing platform based on nickel oxide nanoparticles anchored on MXene, *Microchem. J.*, 193, 109216.

[24] Johannessen, S.I., and Tomson, T., 2006, Pharmacokinetic variability of newer antiepileptic drugs, *Clin. Pharmacokinet*., 45 (11), 1061–1075.

[25] Wissenbach, D.K., Binz, T.M., and Steuer, A.E., 2023, Advances in testing for sample manipulation in clinical and forensic toxicology—part B: Hair samples, *Anal. Bioanal. Chem.*, 415 (21), 5117–5128.

[26] Shu, I., Alexander A., Jones, M., Jones, J., and Negrusz, A., 2016, Determination of methamphetamine enantiomer composition in human hair by non-chiral liquid chromatography–tandem mass spectrometry method, *J. Chromatogr. B*, 1028, 145–152.

[27] McKenzie, E.J., Miskelly, G.M., and Butler, P.A.G., 2013, Dynamic solid phase microextraction analysis for airborne methamphetamine: Quantitation using isotopically substituted methamphetamine, *Anal. Methods*, 5, 4391–4396.

[28] Dos Santos, B.P., Scherer, J.N., Viola, P.P., Govoni, B., Vasconcelos, M., Dalanhol, C.S., Borges, G.R., de Gouveia, G.C., Arantes, A.C.F., Martins, A.F., da Costa, J.L., Huestis, M.A., and Pechansky, F., 2025, Oral fluid device performance in identifying amphetamine, methamphetamine, and cocaine use in Brazilian drivers, *J. Anal. Toxicol.*, 49 (7), 450–459.

[29] Tani, N., Oritani, S., Ono, M., and Ishikawa, T., 2025, Forensic significance of quantitatively analyzing methamphetamine in male reproductive organs, *Leg. Med.*, 75, 102618.

[30] Argente-García, A., Jornet-Martínez, N., Herráez-Hernández, R., and Campíns-Falcó, P., 2016, A solid colorimetric sensor for the analysis of amphetamine-like street samples, *Anal. Chim. Acta*, 943, 123–130.

[31] Wright, J., Kenneally, M., Ross, K., and Walker, S., 2020, Environmental methamphetamine exposures and health effects in 25 case studies, *Toxics*, 8 (3), 61.

[32] Russell, M., Nicolle, S., Mayo, E., and Chappell, A., 2022, Deposition of methamphetamine residues produced by simulated smoking, *Forensic Sci. Int.*, 338, 111407.

[33] Gao, J., Culshaw, P., Ngo, H.K.T., Howell, J., Le, H.H.T.C., Yang, M., and Thai, P.K., 2023, Methamphetamine contamination in residential properties and their remediation in Queensland, Australia, *Forensic Sci. Int.: Rep.*, 7, 100311.

[34] Kerry, G.L., Ross, K.E., Walker, G.S., and Wright, J., 2025, Determining extent and distribution of methamphetamine in cars: Air vs. surface vs. fabrics, *Forensic Chem.*, 42, 100628.

[35] Farst, K., and Bolden, B.B., 2012, Substance-exposed infants and children: forensic approach, *Clin. Pediatr. Emerg. Med.*, 13 (3), 221–228.

[36] Morrison, G., Shakila, N.V., and Parker, K., 2015, Accumulation of gas-phase methamphetamine on clothing, toy fabrics, and skin oil, *Indoor Air*, 25 (4), 405–414.

[37] Krakowiak, R.I., Poklis, J.L., and Peace, M.R., 2019, The analysis of aerosolized methamphetamine from E-cigarettes using high resolution mass spectrometry and gas chromatography mass spectrometry, *J. Anal. Toxicol.*, 43 (8), 592–599.

[38] Bagheri, H., Zavareh, A.F., and Koruni, M.H., 2016, Graphene oxide assisted electromembrane extraction with gas chromatography for the determination of methamphetamine as a model analyte in hair and urine samples, *J. Sep. Sci.*, 39 (6), 1182–1188.

[39] Miraee, S.N., Qomi, M., Shamshiri, F., and Raoufi, P., 2014, Hollow-fiber liquid-phase microextraction followed by high performance liquid chromatography for the determination of trace amounts of methylphenidate hydrochloride in biological fluids, *Biomed. Pharmacol. J.*, 7 (2), 715–725.

[40] Bahmanabadi, L., Akhgari, M., Jokar, F., and Sadeghi, H.B., 2017, Quantitative determination of methamphetamine in oral fluid by liquid–liquid extraction and gas chromatography/mass spectrometry, *Hum. Exp. Toxicol.*, 36 (2), 195–202.

[41] Radwan, R.A., Abouzied, N.F., Mora, A., Hassan, A.M., and Abd Elkader, M.M., 2025, Study of methamphetamine abuse among drug abuse positive cases attending Sohag clinical toxicology laboratory by new validated HPLC-DAD method, *Ain Shams J. Forensic Med. Clin. Toxicol.*, 44, 100–118.

[42] Gracia-Lor, E., Pérez-Valenciano, A., De Oro-Carretero, P., Ramírez-García, L., Sanz-Landaluze, J., and Martín-Gutiérrez, M.J., 2024, Consumption of illicit drugs and benzodiazepines in six Spanish cities during different periods of the COVID-19 pandemic, *Sci. Total. Environ*., 935, 173356.

[43] Kumazawa, T., Hasegawa, C., Hara, K., Uchigasaki, S., Lee, X.P., Seno, H., Suzuki, O., and Sato, K., 2012, Molecularly imprinted solid-phase extraction for the selective determination of methamphetamine, amphetamine, and methylenedioxyphenylalkylamine designer drugs in human whole blood by gas chromatography-mass spectrometry, *J. Sep. Sci*., 35 (5-6), 726–733.

[44] Rezazadeh, M., Yamini, Y., and Seidi, S., 2015, Application of a new nanocarbonaceous sorbent in electromembrane surrounded solid phase microextraction for analysis of amphetamine and methamphetamine in human urine and whole blood, *J. Chromatogr. A*, 1396, 1–6.

[45] Kala, K.L., Anbuchezhiyan, G., Pingili, K., Singh, P.K., Vel, V.M., Yusuf, K., Aljuwayid, A.M., Islam, M.A., and Christopher, D., 2023, Employing a carbon-based nanocomposite as a diffusive solid-phase extraction adsorbent for methamphetamine for therapeutic purposes, *Adsorp. Sci. Technol*., 2023, 8650678.

[46] Farasati Far, B., Naimi-Jamal, M.R., Jahanbakhshi, M., Mohammed, H.T., Altimari, U.S., and Ansari, J., 2022, Poly(3-thienylboronic acid) coated magnetic nanoparticles as a magnetic solid-phase adsorbent for extraction of methamphetamine from urine samples, *J. Dispersion Sci. Technol.*, 44 (14), 2723–2733.

[47] Ghalebi, M., Hamidi, S., Nemati, M., Sheykizadeh, S., Lotfipour, F., Alipour Ghorbani, N., and Farjami, A., 2022, Development of an efficient and sensitive magnetic dispersive solid-phase extraction technique for preconcentration of amphetamine and methamphetamine determined by high-performance liquid chromatography and liquid chromatography-tandem mass spectrometry in sports supplements, *Anal. Bioanal. Chem. Res.*, 9 (4), 431–442.

[48] Simarro-Gimeno, C., Garlito, B., Pitarch, E., and Hernández, F., 2023, Evaluation of direct sample injection as a fast, no-sample handling, approach for the LC-MS/MS monitoring of pharmaceuticals in different water matrices, *Microchem. J*., 193, 108985.

[49] Jørgenrud, B., McQuade, T., Maria, M.H., Nilsson, G., and Berg, T., 2025, Buffer-free high pH mobile phase LC-MS/MS for determination of the alcohol biomarker phosphatidylethanol 16: 0/18: 1 and 20 drugs and metabolites in whole blood, *Talanta*, 282, 126964.

[50] Baz-Lomba, A., Löve, A.S.C., Reid, M.J., Ólafsdóttir, K., and Thomas, K.V., 2018, A high-throughput solid-phase microextraction and post-loop mixing large volume injection method for water samples, *J. Chromatogr. A*, 1531, 32–38.

[51] Boogaerts, T., Quireyns, M., Maes, F., Laimou-Geraniou, M., Van Wichelen, N., Heath, E., Pussig, B., Aertgeerts, B., Covaci, A., and van Nuijs, A.L.N., 2023, Optimization, validation and application of a high-throughput 96-well elution protocol for the quantification of psychoactive substances in influent wastewater, *Drug Test. Anal.*, 15 (2), 240–246.

[52] Vosough, M., Mohamedian, H., Salemi, A., and Baheri, T., 2015, Multivariate curve resolution-assisted determination of pseudoephedrine and methamphetamine by HPLC-DAD in water samples, *J. Chromatogr. Sci*., 53 (2), 233–239.

[53] Abdulrahman, S.K., Qassim, A.W., and Rasheed, A.S., 2022, The evaluation of two zwitterionic hydrophilic interaction liquid chromatography materials for the rapid separation of methamphetamine and muscimol pharmaceuticals, *Int. J. Drug Delivery Technol.*, 12 (2), 1882–1886.

[54] Nourani, N., Javadzadeh, Y., Shayanfar, A., Taghvimi, A., Bavili-Tabrizi, A., and Dastmalchi, S., 2024, Extraction of methamphetamine and pseudoephedrine by modified graphene oxide solid phase extraction method coupled to HPLC-UV in urine sample, *BMC Chem.*, 18 (1), 216.

[55] Zhang, S., Cui, Y., Sun, J., Xi, Y., Zhang, C., and Tang, J., 2015, Sensitive magnetic solid-phase microextraction based on oxide multi-walled carbon-nanotubes for the determination of methylamphetamine and ketamine in human urine and blood, *Anal. Methods*, 7 (10), 4209–4215.

[56] Taghvimi, A., and Hamishehkar, H., 2017, Carbon coated magnetic nanoparticles as a novel magnetic solid phase extraction adsorbent for simultaneous extraction of methamphetamine and ephedrine from urine samples, *J. Chromatogr. B*, 1041-1042, 113–119.

[57] Haeri, S., Abbasi, S., and Sajjadifar, S., 2017, Bio-dispersive liquid liquid microextraction based on nano rhaminolipid aggregates combined with magnetic solid phase extraction using Fe_3O_4@PPy magnetic nanoparticles for the determination of methamphetamine in human urine, *J. Chromatogr. B.*, 1063, 101–106.

[58] Lu, Q., Guo, H., Zhang, Y., Tang, X., Lei, W., Qi, R., Chu, J., Li, D., and Zhao, Q., 2020, Graphene oxide-Fe_3O_4 nanocomposite magnetic solid phase extraction followed by UHPLC-MS/MS for highly sensitive determination of eight psychoactive drugs in urine samples, *Talanta*, 206, 120212.

[59] Akramipour, R., Fattahi, N., Pirsaheb, M., and Gheini, S., 2016, Combination of counter current salting-out homogenous liquid–liquid extraction and dispersive liquid–liquid microextraction as a novel microextraction of drugs in urine samples, *J. Chromatogr. B*, 1012-1013, 162–168.

[60] Chen, X., 2015, Analysis of methamphetamine in human urine using ionic liquid dispersive liquid-phase microextraction combined with HPLC, *Chromatographia*, 78 (7), 515–520.

[61] Wang, R., Qi, X., Zhao, L., Liu, S., Gao, S., Ma, X., and Deng, Y., 2016, Ionic-liquid-based dispersive liquid–liquid microextraction coupled with high-performance liquid chromatography for the forensic determination of methamphetamine in human urine, *J. Sep. Sci.*, 39 (13), 2444–2450.

[62] Alizadeh, N., Jafari, M., and Mohammadi, A., 2009, Headspace-solid-phase microextraction using a dodecylsulfate-doped polypyrrole film coupled to ion mobility spectrometry for analysis methyl tert-butyl ether in water and gasoline, *J. Hazard. Mater.*, 169 (1-3), 861–867.

[63] McKenzie, E.J., Miskelly, G.M., and Butler, P.A.G., 2013, Detection of methamphetamine in indoor air using dynamic solid phase microextraction: A supplementary method to surface wipe sampling, *Anal. Methods*, 5 (20), 5418–5424.

[64] Nair, M.V., and Miskelly, G.M., 2016, Capillary microextraction: A new method for sampling methamphetamine vapour, *Forensic Sci. Int.*, 268, 131–138.

[65] Nair, M.V., and Miskelly, G.M., 2019, Determination of airborne methamphetamine via capillary microextraction of volatiles (CMV) with on-sorbent derivatisation using *o*-pentafluorobenzyl chloroformate, *Forensic Chem.*, 14, 100161.

[66] Dobos, A., Hidvégi, E., and Somogyi, G.P., 2012, Comparison of five derivatizing agents for the determination of amphetamine-type stimulants in Human urine by extractive acylation and gas chromatography–mass spectrometry, *J. Anal. Toxicol.*, 36 (5), 340–344.

[67] Pires, B., Simão, A., Rosado, T., Barroso, M., and Gallardo, E., 2025, Determination of amphetamines in hair samples using microextraction by packed sorbent and gas chromatography–mass spectrometry, *Drug Test. Anal.*, 17 (6), 761–771.

[68] Kwon, N.H., Lee, Y.R., Kim, H.S., Cheong, J.C., and Kim, J.Y., 2019, Hybrid solid-phase extraction for selective determination of methamphetamine and amphetamine in dyed hair by using gas chromatography–mass spectrometry, *Molecules*, 24 (13), 2501.

[69] Han, E., Yang, H., Seol, I., Park, Y., Lee, B., and Song, J.M., 2013, Segmental hair analysis and

estimation of methamphetamine use pattern, *Int. J. Leg. Med.*, 127 (2), 405–411.

[70] Alawi, A., Dhabbah, A.M., Morrison, C., Ben-Jaber, S., AlAngari, W.A., Bin Jassas, M., and Badjah-Hadj-Ahmed, Y., 2023, Indirect chiral separation of crystal methamphetamine seized in Saudi Arabia using GC-MS, *Aust. J. Forensic Sci.*, 55 (6), 731–744.

[71] Djozan, D., Farajzadeh, M.A., Sorouraddin, S.M., and Baheri, T., 2012, Determination of methamphetamine, amphetamine and ecstasy by inside-needle adsorption trap based on molecularly imprinted polymer followed by GC-FID determination, *Microchim. Acta*, 179 (3), 209–217.

[72] Khajeamiri, A.R., Faizi, M., Sohani, F., Baheri, T., and Kobarfard, F., 2012, Determination of impurities in illicit methamphetamine samples seized in Iran, *Forensic Sci. Int.*, 217 (1), 204–206.

[73] Mostafa, I.M., Meng, C., Dong, Z., Lou, B., and Xu, G., 2022, Potentiometric sensors for the determination of pharmaceutical drugs, *Anal. Sci.*, 38 (1), 23–37.

[74] Al-Hetlani, E., 2013, Forensic drug analysis and microfluidics, *Electrophoresis*, 34 (9-10), 1262–1272.

[75] Ammen, E.W., and Al-Bayati, Y.K., 2024, Determination of chlorpromazine using molecular imprinting polymers in different sample matrices, *Indones. J. Chem.*, 24 (6), 1870–1882.

[76] Mao, K., Zhang, H., Wang, Z., Cao, H., Zhang, K., Li, X., and Yang, Z., 2020, Nanomaterial-based aptamer sensors for arsenic detection, *Biosens. Bioelectron.*, 148, 111785.

[77] Krauss, S.T., Remcho, T.P., Lipes, S.M., Aranda, R., Maynard, H.P., Shukla, N., Li, J., Tontarski, R.E., and Landers, J.P., 2016, Objective method for presumptive field-testing of illicit drug possession using centrifugal microdevices and smartphone analysis, *Anal. Chem.*, 88 (17), 8689–8697.

[78] Guo, J., Tian, S., Liu, K., and Guo, J., 202i, IoT-enabled fluorescence sensor for quantitative KET detection and anti-drug situational awareness, *IEEE Trans. NanoBiosci.*, 20 (1), 2–8.

[79] Fan, L., Yang, J., Wu, J., Li, F., Yan, W., Tan, F., Zhang, M., Draz, M.S., Han, H., and Zhang, P., 2022, Deeply-dyed nanobead system for rapid lateral flow assay testing of drugs at point-of-care, *Sens. Actuators, B*, 362, 131829.

[80] He, C., He, Q., Deng, C., Shi, L., Fu, Y., Cao, H., and Cheng, J., 2011, Determination of methamphetamine hydrochloride by highly fluorescent polyfluorene with NH_2-terminated side chains, *Synth. Met.*, 161 (3-4), 293–297.

[81] Wen, D., Fu, Y.Y., Shi, L.Q., He, C., Dong, L., Zhu, D.F., He, Q.G., Cao, H.M., and Cheng, J.G., 2012, Fine structural tuning of fluorescent copolymer sensors for methamphetamine vapor detection, *Sens. Actuators, B*, 168, 283–288.

[82] Rouhani, S., and Haghgoo, S., 2015, A novel fluorescence nanosensor based on 1,8-naphthalimide-thiophene doped silica nanoparticles, and its application to the determination of methamphetamine, *Sens. Actuators, B*, 209, 957–965.

[83] Dennis, A.M., Rhee, W.J., Sotto, D., Dublin, S.N., and Bao, G., 2012, Quantum dot–fluorescent protein FRET probes for sensing intracellular pH, *ACS Nano*, 6 (4), 2917–2924.

[84] Mohammad-Rezaei, R., and Razmi, H., 2012, Reduced graphene oxide|carbon ceramic electrode modified with CdS-hemoglobin as a sensitive hydrogen peroxide biosensor, *Electroanalysis*, 24 (11), 2094–2101.

[85] Roushani, M., and Shahdost-Fard, F., 2017, Ultra-sensitive detection of ibuprofen (IBP) by electrochemical aptasensor using the dendrimer-quantum dot (Den-QD) bioconjugate as an immobilization platform with special features, *Mater. Sci. Eng., C*, 75, 1091–1096.

[86] Masteri-Farahani, M., and Mosleh, N., 2019, Modified CdS quantum dots as selective turn-on fluorescent nanosensor for detection and determination of methamphetamine, *J. Mater. Sci.: Mater. Electron.*, 30 (24), 21170–21176.

[87] Shen, J., Zhu, Y., Yang, X., and Li, C., 2012, Graphene quantum dots: Emergent nanolights for bioimaging, sensors, catalysis and photovoltaic devices, *Chem. Commun.*, 48 (31), 3686–3699.

[88] Akhoundian, M., Alizadeh, T., Ganjali, M.R., and Norouzi, P., 2019, Ultra-trace detection of

methamphetamine in biological samples using FFT-square wave voltammetry and nano-sized imprinted polymer/MWCNTs-modified electrode, *Talanta*, 200, 115–123.

[89] Masteri-Farahani, M., Mashhadi-Ramezani, S., and Mosleh, N., 2020, Molecularly imprinted polymer containing fluorescent graphene quantum dots as a new fluorescent nanosensor for detection of methamphetamine, *Spectrochim. Acta, Part A*, 229, 118021.

[90] Mandani, S., Rezaei, B., and Ensafi, A.A., 2020, Sensitive imprinted optical sensor based on mesoporous structure and green nanoparticles for the detection of methamphetamine in plasma and urine, *Spectrochim. Acta, Part A*, 231, 118077.

[91] Goulding, W., Sun, Y., and Ashley, J., 2025, NanoMIP beacons with a co-operative binding mechanism for the all-in-one detection of methamphetamine aptamer complexes, *Biosens. Bioelectron*., 267, 116856.

[92] Saberi, Z., Rezaei, B., Faroukhpour, H., and Ensafi, A.A., 2018, A fluorometric aptasensor for methamphetamine based on fluorescence resonance energy transfer using cobalt oxyhydroxide nanosheets and carbon dots, *Microchim. Acta*, 185 (6), 303.

[93] Li, B., Li, K., Xu, W., Yan, M., Zhao, J., Zhang, W., Yuan, M., Fu, Y., He, Q., and Cheng, J., 2023, Micro-interfaces modulation by UV—ozone substrate treatment for MPEA vapor fluorescence detection, *Nano Res.*, 16 (3), 4055–4060.

[94] Liu, K., Shang, C., Wang, Z., Qi, Y., Miao, R., Liu, K., Liu, T., and Fang, Y., 2018, Non-contact identification and differentiation of illicit drugs using fluorescent films, *Nat. Commun.*, 9 (1), 1695.

[95] Zhang, Y., Bunes, B.R., Wu, N., Ansari, A., Rajabali, S., and Zang, L., 2018, Sensing methamphetamine with chemiresistive sensors based on polythiophene-blended single-walled carbon nanotubes, *Sens. Actuators, B*, 255, 1814–1818.

[96] Elmizadeh, H., Bardajee, G.R., and Moaddeli, A., 2023, Ultrasensitive and rapid detection of methamphetamine in forensic biological fluids using fluorescent apta-nanobiosensors based on CdTe quantum dots, *Microchem. J.*, 189, 108519.

[97] Ghorbanizamani, F., Moulahoum, H., and Timur, S., 2021, Noninvasive optical sensor for the detection of cocaine and methamphetamine in saliva using rhodamine B-labeled polymersomes, *IEEE Sens. J.*, 22 (2), 1146–1153.

[98] Awata, S., Kikuchi, F., and Oba, T., 2025, Naked-eye sensor for rapid methamphetamine screening with analyte recovery, *Forensic Chem.*, 42, 100634.

[99] Xiao, R., Wang, D., Lin, Z., Qiu, B., Liu, M., Guo, L., and Chen, G., 2015, Disassembly of gold nanoparticle dimers for colorimetric detection of ochratoxin A, *Anal. Methods*, 7 (3), 842–845.

[100] Petryayeva, E., and Krull, U.J., 2011, Localized surface plasmon resonance: Nanostructures, bioassays and biosensing—A review, *Anal. Chim. Acta*, 706 (1), 8–24.

[101] Yarbakht, M., and Nikkhah, M., 2016, Unmodified gold nanoparticles as a colorimetric probe for visual methamphetamine detection, *J. Exp. Nanosci.*, 11 (7), 593–601.

[102] Shi, Q., Shi, Y., Pan, Y., Yue, Z., Zhang, H., and Yi, C., 2015, Colorimetric and bare eye determination of urinary methylamphetamine based on the use of aptamers and the salt-induced aggregation of unmodified gold nanoparticles, *Microchim. Acta*, 182 (3), 505–511.

[103] Mao, K., Yang, Z., Li, J., Zhou, X., Li, X., and Hu, J., 2017, A novel colorimetric biosensor based on non-aggregated Au@Ag core–shell nanoparticles for methamphetamine and cocaine detection, *Talanta*, 175, 338–346.

[104] Mao, K., Ma, J., Li, X., and Yang, Z., 2019, Rapid duplexed detection of illicit drugs in wastewater using gold nanoparticle conjugated aptamer sensors, *Sci. Total. Environ.*, 688, 771–779.

[105] Adegoke, O., Zolotovskaya, S., Abdolvand, A., and Daeid, N.N., 2020, Biomimetic graphene oxide-cationic multi-shaped gold nanoparticle-hemin hybrid nanozyme: Tuning enhanced catalytic activity for the rapid colorimetric apta-biosensing

of amphetamine-type stimulants, *Talanta*, 216, 120990.

[106] Bastami, T.R., Ghamari, Y., Khadempir, S., Khorasani, M.E., Paolesse, R., and Bayat, M., 2024, Discriminative detection of morphine and methamphetamine-like street samples by label-free Cu doped-silver nanoparticles chemosensor, *J. Ind. Eng. Chem.*, 131, 459–469.

[107] Zagatto, E.A.G., Oliveira, C.C., Townshend, A., and Worsfold, P., 2012, *Flow Analysis with Spectrophotometric and Luminometric Detection*, Elsevier, Amsterdam, Netherlands.

[108] Wang, Z., Dong, B., Feng, G., Shan, H., Huan, Y., and Fei, Q., 2019, Water-soluble hemin-mPEG-enhanced luminol chemiluminescence for sensitive detection of hydrogen peroxide and glucose, *Anal. Sci.*, 35 (10), 1135–1140.

[109] Zhao, S., Chen, X., Huang, J., Zhang, X., Sun, J., and Yang, L., 2022, Point-of-care testing of methylamphetamine with a portable optical fiber immunosensor, *Anal. Chim. Acta*, 1192, 339345.

[110] Hassanzadeh, J., Khataee, A., and Lotfi, R., 2017, Sensitive fluorescence and chemiluminescence procedures for methamphetamine detection based on CdS quantum dots, *Microchem. J.*, 132, 371–377.

[111] Rosy, R., Yadav, S.K., Agrawal, B., Oyama, M., and Goyal, R.N., 2014, Graphene modified palladium sensor for electrochemical analysis of norepinephrine in pharmaceuticals and biological fluids, *Electrochim. Acta*, 125, 622–629.

[112] Roushani, M., Dizajdizi, B.Z., Salimi, A., and Azadbakht, A., 2019, Preparation of modified glassy carbon electrode by the use of titanium oxide, copper and palladium nanoparticles and its application for the electrocatalytic and photelectrocatalytic reduction of hydrogen peroxide, *J. Mater. Sci.: Mater. Electron.*, 30 (5), 5212–5221.

[113] Razmi, H., Ezzati, L., and Khorablou, Z., 2019, Direct electrochemical synthesis of graphene oxide/cobalt oxide nanocomposite on pencil graphite electrode for highly sensitive and selective detection of insulin in pharmaceutical samples, *J. Electrochem. Soc.*, 166 (12), B961.

[114] Karim-Nezhad, G., Khorablou, Z., and Dorraji, P.S., 2016, Modification of glassy carbon electrode with a bilayer of multiwalled carbon nanotube/poly (l-arginine) in the presence of surfactant: Application to discrimination and simultaneous electrochemical determination of dihydroxybenzene isomers, *J. Electrochem. Soc.*, 163 (7), B358.

[115] Baghbamidi, S.E., Beitollahi, H., Tajik, S., and Hosseinzadeh, R., 2016, Voltammetric sensor based on 1-benzyl-4-ferrocenyl-1*H*-[1,2,3]-triazole/carbon nanotube modified glassy carbon electrode; detection of hydrochlorothiazide in the presence of propranolol, *Int. J. Electrochem. Sci.*, 11 (12), 10874–10883.

[116] Rezaei, B., and Irannejad, N., 2019, "Electrochemical detection techniques in biosensor applications" in *Electrochemical Biosensors*, Eds. Ensafi, A.A., Elsevier, Amsterdam, Netherlands, 11–43.

[117] Kohzadi, R., Molaeirad, A., Alijanianzadeh, M., Kamali, N., and Mohtashamifar, M., 2016, Designing a label free aptasensor for detection of methamphetamine, *Biomacromol. J.*, 2 (1), 28–33.

[118] Švorc, Ľ., Vojs, M., Michniak, P., Marton, M., Rievaj, M., and Bustin, D., 2014, Electrochemical behavior of methamphetamine and its voltammetric determination in biological samples using self-assembled boron-doped diamond electrode, *J. Electroanal. Chem.*, 717-718, 34–40.

[119] Oghli, A.H., Alipour, E., and Asadzadeh, M., 2015, Development of a novel voltammetric sensor for the determination of methamphetamine in biological samples on the pretreated pencil graphite electrode, *RSC. Adv.*, 5 (13), 9674–9682.

[120] Bartlett, C.A., Taylor, S., Fernandez, C., Wanklyn, C., Burton, D., Enston, E., Raniczkowska, A., Black, M., and Murphy, L., 2016, Disposable screen printed sensor for the electrochemical detection of methamphetamine in undiluted saliva, *Chem. Cent. J.*, 10 (1), 3.

[121] Razmi, H., Sarhang-Zadeh, K., and Mohammad-Rezaei, R., 2013, Electrochemical behavior and voltammetric determination of diclofenac at a

multi-walled carbon nanotube-ionic liquid composite modified carbon ceramic electrode, *Anal. Lett.*, 46 (12), 1885–1896.

[122] Demir, B., Yilmaz, T., Guler, E., Gumus, Z.P., Akbulut, H., Aldemir, E., Coskunol, H., Colak, D.G., Cianga, I., Yamada, S., Timur, S., Endo, T., and Yagci, Y., 2016, Polypeptide with electroactive endgroups as sensing platform for the abused drug 'methamphetamine' by bioelectrochemical method, *Talanta*, 161, 789–796.

[123] Dokuzparmak, E., Brown, K., and Dennany, L., 2021, Electrochemiluminescent screening for methamphetamine metabolites, *Analyst*, 146 (10), 3336–3345.

[124] Xie, Y., Wu, S., Chen, Z., Jiang, J., and Sun, J., 2022, Rapid nanomolar detection of methamphetamine in biofluids via a reagentless electrochemical aptamer-based biosensor, *Anal. Chim. Acta*, 1207, 339742.

[125] Ghorbanizamani, F., Moulahoum, H., Guler Celik, E., and Timur, S., 2022, Ionic liquid-hydrogel hybrid material for enhanced electron transfer and sensitivity towards electrochemical detection of methamphetamine, *J. Mol. Liq.*, 361, 119627.

[126] Beduk, D., Beduk, T., de Oliveira Filho, J.I., Ait Lahcen, A., Aldemir, E., Guler Celik, E., Salama, K.N., and Timur, S., 2023, Smart multiplex point-of-care platform for simultaneous drug monitoring, *ACS. Appl. Mater. Interfaces*, 15 (31), 37247–37258.

[127] Haghighi, M., Shahlaei, M., Irandoust, M., and Hassanpour, A., 2020, New and sensitive sensor for voltammetry determination of methamphetamine in biological samples, *J. Mater. Sci.: Mater. Electron.*, 31 (14), 10989–11000.

[128] Anvari, L., Ghoreishi, S.M., Faridbod, F., and Ganjali, M.R., 2021, Electrochemical determination of methamphetamine in human plasma on a nanoceria nanoparticle decorated reduced graphene oxide (rGO) glassy carbon electrode (GCE), *Anal. Lett.*, 54 (15), 2509–2522.

[129] Riahifar, V., Haghnazari, N., Keshavarzi, F., and Ahmadi, E., 2021, A sensitive voltammetric sensor for methamphetamine determination based on modified glassy carbon electrode using Fe_3O_4@poly pyrrole core-shell and graphene oxide, *Microchem. J.*, 170, 106748.

[130] Cetó, X., Truta, F.M., Dragan, A.M., Rodríguez-Franch, E., Tertis, M., Sánchez-Pereña, Á., Comellas-Tena, S., Cristea, C., and del Valle, M., 2025, Towards the development of a portable device based on modified-voltammetric sensors for the detection of illicit drugs and seized samples, *Talanta*, 282, 127055.

[131] Lee, K., Saisahas, K., Soleh, A., Kunalan, V., Chang, K.H., Limbut, W., and Abdullah, A.F.L., 2022, Forensic electrochemistry: Electrochemical analysis of trace methamphetamine residues on household surfaces, *J. Electrochem. Soc.*, 169 (5), 056514.

[132] Liu, H., 2024, Highly selective detection of methamphetamine in urine using biosynthesized graphene oxide-gold nanoparticle composite modified electrodes, *Int. J. Electrochem. Sci.*, 19 (11), 100851.

[133] Sun, H., Liu, J., Qiu, Y., Kong, J., and Zhang, X., 2022, High sensitive electrochemical methamphetamine detection in serum and urine via atom transfer radical polymerization signal amplification, *Talanta*, 238, 123026.

[134] Duan, S., Chen, H., Xu, A., He, Y., Li, M., Zhang, R., Zhang, R., and Bai, H., 2024, A simple polyarginine membrane electrochemical sensor for the determination of MDMA and MDA, *Anal. Biochem.*, 688, 115478.

[135] Anzar, N., Suleman, S., Singh, Y., Parvez, S., Khanuja, M., Pilloton, R., and Narang, J., 2023, Wearable electrochemical glove-based analytical device (eGAD) for the detection of methamphetamine employing silver nanoparticles, *Biosensors*, 13 (10), 934.

[136] Anzar, N., Suleman, S., Bano, H., Parvez, S., Khanuja, M., Pilloton, R., and Narang, J., 2023, Paper-based electrodes decorated with silver and zinc oxide nanocomposite for electro-chemical sensing of methamphetamine, *Sensors*, 23 (12), 5519.

[137] Suleman, S., Anzar, N., Patil, S., Ansari, S., Jahan, F., and Narang, J., 2025, Development of an

electrochemical paper based multiplex analytical device for the detection of "illicit drugs" employing silver nanoparticles, *Mater. Chem. Phys.*, 338, 130649.

[138] Saisahas, K., Soleh, A., Somsiri, S., Senglan, P., Promsuwan, K., Saichanapan, J., Kanatharana, P., Thavarungkul, P., Lee, K., Chang, K.H., Abdullah, A.F.L., Tayayuth, K., and Limbut, W., 2022, Electrochemical sensor for methamphetamine detection using laser-induced porous graphene electrode, *Nanomaterials*, 12 (1), 73.

[139] Zhao, B., Wang, C., Huang, J., and Zhang, J., 2025, Wood-derived ionic conductive cellulose for transparent and flexible methamphetamine analog sensors, *ACS Omega*, 10 (17), 17770–17776.

[140] Watanabe, K., Okada, K., and Katsu, T., 1993, Determination of methamphetamine in urine in situ using a methamphetamine-sensitive membrane electrode, *Anal. Chim. Acta*, 274 (1), 59–63.

[141] Hayat, A., Catanante, G., and Marty, J.L., 2014, Current trends in nanomaterial-based amperometric biosensors, *Sensors*, 14 (12), 23439–23461.

[142] Zhang, L.Y., and Liu, Y.J., 2014, Label-free amperometric immunosensor based on Prussian blue as artificial peroxidase for the detection of methamphetamine, *Anal. Chim. Acta*, 806, 204–209.

[143] Randviir, E.P., and Banks, C.E., 2013, Electrochemical impedance spectroscopy: An overview of bioanalytical applications, *Anal. Methods*, 5 (5), 1098–1115.

[144] Yeh, C.H., Wang, W.T., Shen, P.L., and Lin, Y.C., 2012, A developed competitive immunoassay based on impedance measurements for methamphetamine detection, *Microfluid. Nanofluid.*, 13 (2), 319–329.

[145] Yang, Y., Pan, J., Hua, W., and Tu, Y., 2014, An approach for the preparation of highly sensitive electrochemical impedimetric immunosensors for the detection of illicit drugs, *J. Electroanal. Chem.*, 726, 1–6.

[146] Ebrahimi, M., Johari-Ahar, M., Hamzeiy, H., Barar, J., Mashinchian, O., and Omidi, Y., 2012, Electrochemical impedance spectroscopic sensing of methamphetamine by a specific aptamer, *BioImpacts*, 2, 91.

[147] Anvari, L., Ghoreishi, S.M., Khoshnevisan, K., Ganjali, M.R., and Faridbod, F., 2023, Methamphetamine determination using label-free impedimetric aptasensor based on ceria nanocomposite, *J. Appl. Electrochem.*, 53 (9), 1843–1851.

[148] Khorablou, Z., Shahdost-fard, F., and Razmi, H., 2022, Nanodiamond-derived carbon nano-onions decorated with silver nanodendrites as an effective sensing platform for methamphetamine detection, *Surf. Interfaces*, 31, 102061.

[149] Rafiee, B., Fakhari, A.R., and Ghaffarzadeh, M., 2015, Impedimetric and stripping voltammetric determination of methamphetamine at gold nanoparticles-multiwalled carbon nanotubes modified screen printed electrode, *Sens. Actuators, B*, 218, 271–279.

[150] Melo, L.M., de Faria, L.V., Arantes, L.C., Richter, E.M., Munoz, R.A.A., and dos Santos, W.T.P., 2024, Combined colorimetric and electrochemical screening method using 3D printed devices: Towards the selective detection of MDMA in forensic samples, *Electrochim. Acta*, 483, 144041.

[151] Dragan, A.M., Parrilla, M., Sleegers, N., Slosse, A., Van Durme, F., van Nuijs, A., Oprean, R., Cristea, C., and De Wael, K., 2023, Investigating the electrochemical profile of methamphetamine to enable fast on-site detection in forensic analysis, *Talanta*, 255, 124208.