REVIEW

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# Drug Sensors for Detecting Illegal Substances: Mechanisms, Materials, and Detection Methods

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**ABSTRACT:** Globally, the use of illicit drugs is a significant issue that requires the development of sophisticated sensing technology for rapid and accurate detection. This review covers the mechanisms, materials, and applications of modern drug sensors, focusing on four substances: gamma-hydroxybutyrate (GHB), cocaine, fentanyl, and heroin. Optical sensors utilizing fluorescence-based hydroxyphenylbenzothiazole probes make dual-mode detection of GHB in beverages possible, offering real-time analysis with high sensitivity. Electrochemical platforms, such as the microfluidic electrochemical aptamer-based sensor, achieve nanomolar-level cocaine detection in undiluted blood serum through aptamer conformational changes monitored by square wave voltammetry. Material innovations, including ionic liquid-modified electrodes and molecularly imprinted polymers, enhance sensor selectivity and stability in complex composites. The gap between laboratory precision and practical usefulness is filled by portable technologies, such as smartphone-integrated potentiostats for fentanyl screening and 3D-printed micro liquid–liquid interface devices for heroin detection. Even with improvements, issues in reducing interference from intricate sample composition, enhancing environmental stability, and expanding cost-effective production remain. CRISPR-based biosensors and AI-driven signal processing are potential future directions to address new medication trends and support public health initiatives.

**KEYWORDS:** *Drug sensors, GHB, Cocaine, Fentanyl, Heroin, Amphetamine, Methamphetamine, MDMA, Morphine, Oxycodone, Hydrocodone, LSD, Psilocybin, Mescaline, DMT, Marijuana*

## 1. INTRODUCTION

The need for sophisticated detection technologies that combine rapid reaction time, mobility, and high accuracy has increased owing to the spread of illegal drugs, especially synthetic opioids and stimulants. Because they require trained professionals and complex facilities, traditional analytical techniques, such as mass spectrometry and gas chromatography, are only suitable for laboratory settings and are not practical for real-time field applications. This restriction has prompted the development of novel drug sensors aimed at reducing the gap between on-site practicality and laboratory-grade precision [1-4]. Recent advancements in sensor technology have employed optical and electrochemical mechanisms to overcome these challenges. For instance, fluorescence-based optical sensors utilize probes, such as hydroxyphenylbenzothiazole (HBT) derivatives, for GHB detection in beverages, making dual-mode qualitative and quantitative analyses possible through UV-induced fluorescence and colorimetric changes. Electrochemical platforms, such as microfluidic electrochemical aptamer-based sensor (MECAS) systems, achieve nanomolar-level cocaine detection in undiluted blood serum by monitoring conformational changes in methylene blue (MB)-labeled DNA aptamers using square wave voltammetry. These systems are the leading instances of the trend toward compact-designed rapid sensing platforms that give priority to real-time data collection [5-9].

Fig. 1 highlights the growing research interest in drug detection technologies by showing the annual publications and citations related to GHB, cocaine, fentanyl, and heroin from 2015 to 2024. The data demonstrate a significant increase in fentanyl-related publications since 2020, reflecting its central role in overdose fatalities. Similarly, cocaine and

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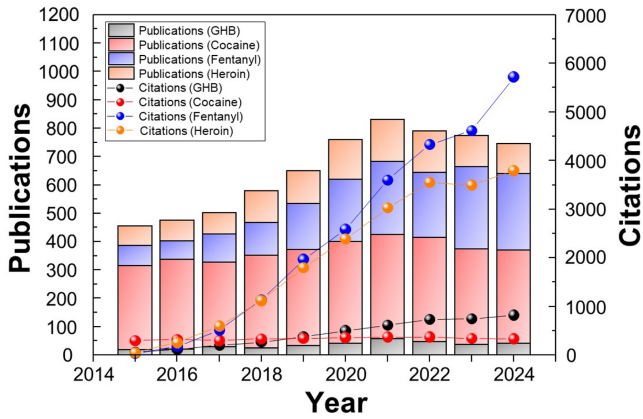


**Fig. 1.** Annual publications and citations related to GHB, cocaine, fentanyl, and heroin, showing the growing research interest in drug detection technologies. The data were collected from the Web of Science using relevant keywords for each substance. Publications are represented as stacked bars, while citations are represented as lines with distinct markers for each drug, providing a clear visualization of citations over time.

heroin research citations have steadily increased, emphasizing the need for advanced detection methods capable of addressing these substances in diverse environments.

Modifications in materials are essential for improving sensor performance. While molecularly imprinted polymers (MIPs) imitate natural receptors to extract heroin from contaminated street samples more strongly, nanoscale modifications, such as ionic liquid-coated screen-printed carbon electrodes (SPCEs) increase the electron transfer kinetics for fentanyl detection. When combined with biorecognition components, such as synthetic antibodies and aptamers, these materials make accurate molecular targeting possible, even in complicated mixtures, such as wastewater or saliva. In addition, portable systems emphasize the connection between nanotechnology and microfluidics [10-13].

Smartphone-integrated potentiostats convert electrochemical signals into useful information for field workers, while 3D-printed micro liquid–liquid interface (μLLI) devices make it easier to quantify heroin in microliter amounts. These technologies not only overcome the drawbacks of conventional approaches but also satisfy the increasing demand for global drug monitoring in prevention and law enforcement [14-16]. Focusing on GHB, cocaine, fentanyl, and heroin, this article covers the material modifications, practical applications, and mechanistic foundations that support the development of contemporary drug sensors. The ways in which diverse advancements in nanoengineering, biorecognition, and device integration are changing the field of illegal substance detection are demonstrated by surveying state-of-the-art research.

## 2. DETECTION MECHANISMS FOR ILLEGAL SUBSTANCES

### 2.1 Optical Detection Mechanisms

Optical detection mechanisms are widely used in drug sensing because of their ability to provide rapid, noninvasive, and highly sensitive analysis. These methods rely on light–matter interactions, such as fluorescence or colorimetric changes, to identify specific substances.

Recognition of GHB, a substance frequently present in beverages, is a well-known example. Molecular probes used in optical sensors have distinctive optical reactions when they interact with GHB, making real-time qualitative and quantitative analyses possible. Fig. 2 shows the dual-mode optical sensor designed to detect GHB in beverages. This sensor utilizes HBT derivatives as fluorescent probes, which emit fluorescence proportional to the concentration of GHB upon exposure to UV light ($\lambda_{ex}$ = 490 nm). The molecular structure of the HBT probe enables it to interact with GHB selectively through hydrogen bonding, disrupting the excited-state intramolecular proton transfer (ESIPT) mechanism of the probe and enhancing the fluorescence intensity. The fluorescence emission spectra show a systematic increase in intensity with increasing GHB concentrations, ranging from 0 to 180 mM. A calibration curve shows a linear response ($R^2$ = 0.9954) across clinically relevant concentrations, with a limit of detection of 0.5 mM. This dual-mode sensor offers significant advantages for field applications. Its fluorescence-based quantitative analysis and visible colorimetric verification under UV light make it highly versatile and adaptable. Furthermore, prompt results for direct beverage screening are guaranteed by the fast response time (less than 2 min). However, a number of difficulties remain. Fluorescence signals may be attenuated by matrix effects from dense or strongly colored beverages, which in certain situations may require sample dilution or pretreatment [5]. Furthermore, outdoor applications may require controlled conditions or portable shielding equipment owing to ambient light interference. Further research should focus on combining this optical sensor with scanners that run on smartphones so that RGB color space algorithms can be used for quantitative analysis. Moreover, the development of near-infrared fluorescence probes, which can reduce matrix interference in complex beverage samples, would increase the application of this technology [4,6,17].

### 2.2 Electrochemical Detection Mechanisms

Electrochemical detection mechanisms are highly effective for drug sensing because of their sensitivity, portability, and com-

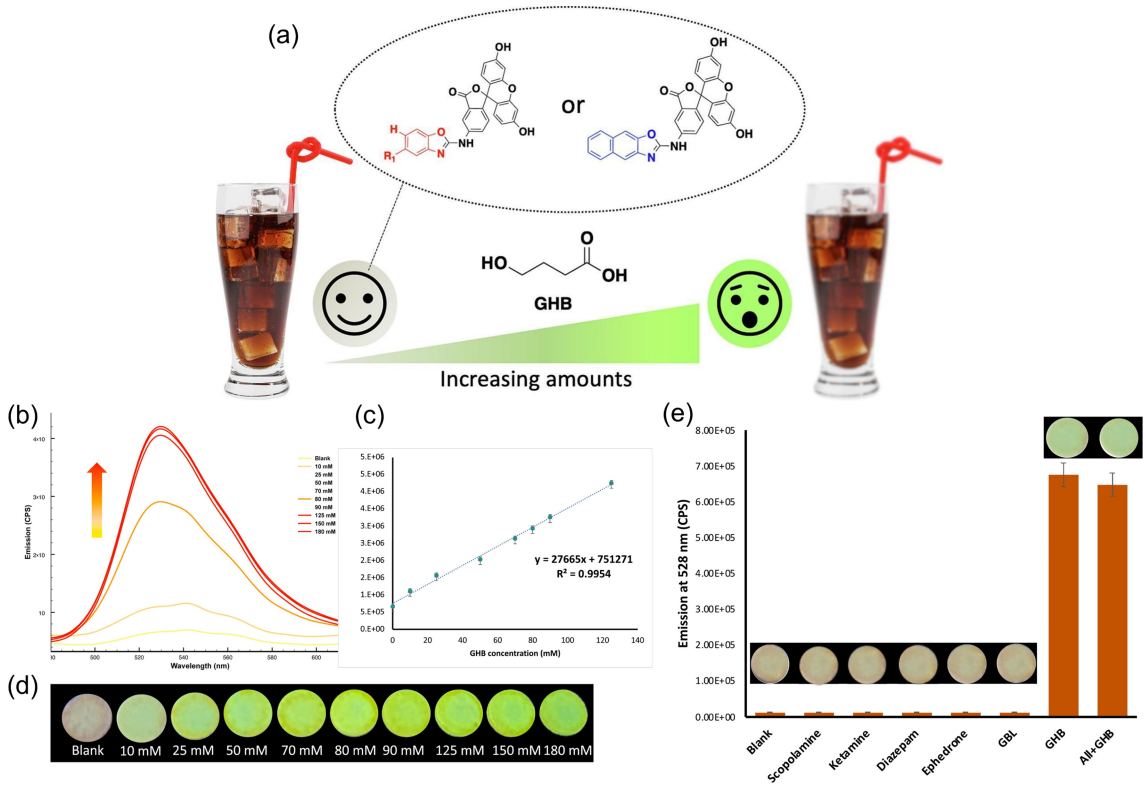


**Fig. 2.** Dual-mode optical sensor for GHB detection. (a) Schematic diagram of the sensing mechanism using HBT-based probes, showing fluorescence enhancement proportional to GHB concentration. (b) Fluorescence emission spectra ($\lambda_{exc}$ = 490 nm, $\lambda_{em}$ = 528 nm) with increasing GHB concentrations (0–180 mM). (c) Calibration curve of emission intensity at 528 nm versus GHB concentration, showing excellent linearity ($R^2$ = 0.9954). (d) Visual fluorescence response to increasing GHB concentrations under UV light. (e) Selectivity test showing strong fluorescence response to GHB and GBL, with negligible interference from other drugs of abuse (15 mM). Reproduced with permission from a previous report [5]. Copyright 2024 Elsevier.

patibility with complex biological systems. These systems measure changes in electrical signals, such as currents or potentials, induced by redox reactions or ion transfer processes upon interaction with target analytes. Fig. 3 depicts the MECAS platform for cocaine detection in undiluted blood serum. This system integrates a microfluidic chip with a 750-nL detection chamber and three electrodes: working (gold), reference (Ag/AgCl), and counter (platinum). MB-labeled DNA aptamers deposited on the working electrode surface are used in the aptamer-based recognition system. When cocaine is not present, these aptamers fold into a hairpin form that transfers electrons by bringing MB close to the electrode surface. Conformational changes of the aptamers upon interacting with cocaine molecules cause MB to be displaced from the electrode surface, decreasing the efficiency of electron transfer [7,18,19].

The microfabricated chip design shows integrated electrodes and fluidic spaces for continuous sample flow. Real-time amperometric responses demonstrate a decrease in current proportional to cocaine concentration over a range of 0–100 μM. Selectivity tests confirmed minimal cross-reactivity with common cutting agents, such as lidocaine or benzoylecgonine. This electrochemical sensor outperforms traditional testing in terms of sensitivity and specificity, achieving a limit of detection in serum samples as low as 10 nM. It is appropriate for clinical and forensic applications because of its microfluidic design, which makes continuous monitoring of cocaine kinetics possible without the need for sample preparation. Despite these advantages, such challenges as electrode fouling caused by protein adsorption in serum and temperature sensitivity affecting aptamer binding kinetics must be addressed to improve long-term performance. Machine-learning (ML) methods may be used in future developments to adjust for variations in the pH and ionic strength of unprocessed samples. Furthermore, the use of this platform in clinical diagnostics and law enforcement may be expanded by incorporating it into wearable technologies that can transmit data wirelessly [20-22].

## 3. MATERIALS FOR DRUG SENSING

### 3.1 Receptors

The ability of receptors to distinguish target analytes from

chemically similar molecules is critical for the selectivity of drug sensors. For example, heroin is often mixed with coffee or paracetamol, making its identification more difficult. By mimicking the lock-and-key specificity of biological receptors, MIPs provide 95% recovery rates in saliva samples that have been interfered with. After the template is removed, these artificial receptors are made by polymerizing functional monomers around a target drug molecule to form 3D cavities that exactly match the size, shape, and functional groups of the analyte [11,14,23].

In addition to MIPs, other recognition components include aptamers, which are synthetic oligonucleotides that change their conformation upon binding. As Fig. 3 shows, the aptamers are especially useful for cocaine detection. Through electrochemical signal transduction, the DNA aptamers tagged with MB exhibit remarkable sensitivity. Using excited-state intramolecular proton transfer mechanisms, HBT derivatives function as fluorescent probes for GHB detection, making dual-mode detection possible through visible color changes and fluorescence enhancement. The stability of these receptors under harsh environmental conditions represents a significant advantage over traditional biological antibodies, which often denature or degrade outside controlled laboratory settings. MIP-based sensors are suitable for forensic applications because of their stability because natural specimens may contain cutting compounds or degradation products that are intended to prevent detection. Computational methods for improving the architecture of MIP binding sites are recent developments that have improved the ability to distinguish target drugs from structurally similar molecules [7,18,19,24,25].

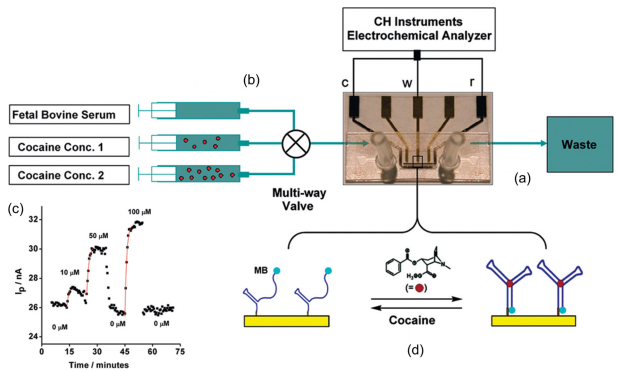


**Fig. 3.** Integrated microfluidic MECAS platform for real-time cocaine detection in continuously flowing undiluted blood serum. (a) The MECAS chip featuring a 750-nL detection chamber with integrated counter (c), working (w), and reference (r) electrodes. (b) Schematic representation of the experimental setup with syringe pumps connected to a multi-way valve enabling sequential sample introduction into the microfluidic device. (c) Real-time amperometric response demonstrating cocaine detection at clinically relevant concentrations (0–100 μM) in flowing blood serum, with clear signal steps observed during concentration modulation. (d) Molecular mechanism of the electrochemical aptamer-based sensor, illustrating the conformational change of the MB-labeled aptamer upon cocaine binding, which alters electron transfer efficiency between the MB redox tag and the electrode surface. This system demonstrates robust performance in complex biofluids without sample pretreatment, displaying potential for drug monitoring application. Reproduced with permission from a previous report [10]. Copyright 2009 American Chemical Society.

### 3.2 Electrode Materials and Modifications

The stability and sensitivity of the electrode are critical under challenging conditions. When fentanyl is detected in street samples, ionic liquid-modified screen-printed electrodes (Fig. 4) show a 5× increase in sensitivity compared with their unmodified counterparts. These developments are essential for immigration organizations that filter illegal shipments because incorrect negative results could result in deadly doses in communities. As shown in Fig. 4, the portable electrochemical sensing platform employs SPCEs modified with ionic liquids to enhance the electron transfer kinetics.

Cyclic square wave voltammetry (CSWV), direct electrochemical analysis using a portable potentiostat, and sample solubilization are all included in the procedure to create distinctive fingerprints. Two separate oxidation peaks for fentanyl, most notably the A2 peak at approximately −0.2 V, demonstrate high linearity ($R^2$ = 0.997) across a concentration range of 0–95 μM, demonstrating the exceptional analytical

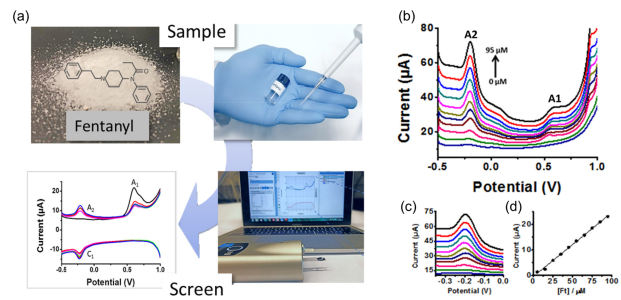


**Fig. 4.** Portable electrochemical sensing platform for fentanyl detection using SPCEs. (a) Workflow for on-site fentanyl detection: solubilization of an unknown sample, direct electrochemical analysis using a portable potentiostat, and identification via CSWV fingerprints. (b) CSWV response of ionic liquid-modified SPCEs to increasing fentanyl concentrations (0–95 μM), showing two characteristic oxidation peaks. (c) Magnified view of the A2 peak at approximately −0.2 V, demonstrating current enhancement with increasing fentanyl concentration. (d) Calibration curve of A2 peak current versus fentanyl concentration, showing excellent linearity ($R^2$ = 0.997). This system offers rapid, sensitive detection suitable for field applications. Reproduced with permission from a previous report [10]. Copyright 2019 American Chemical Society.

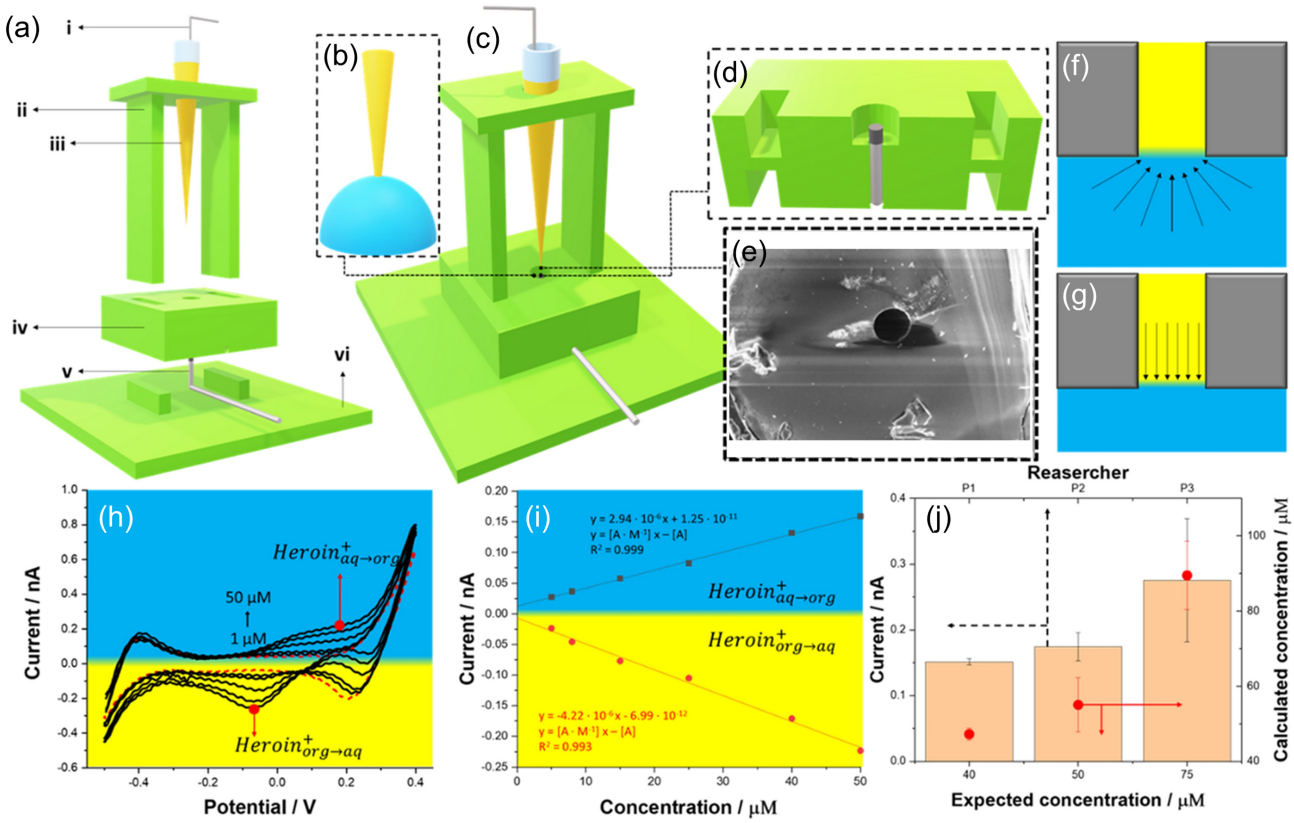


**Fig. 5.** 3D-printed miniaturized platform for electrochemical heroin detection at a μLLI. (a) Schematic of the 3D-printed device, showing: (i) sample inlet, (ii) upper support structure, (iii) microcapillary holder, (iv) lower support structure, (v) base platform, and (vi) electrode connections. (b, c) Expanded and assembled views of the platform, featuring Ag/AgTPBCl (organic phase) and Ag/AgCl (aqueous phase) electrodes, a microcapillary support, and a stable base for precise microliter-volume analysis (d, e) Cross-sectional view and scanning electron microscopy micrograph showing the 25-μm-diameter fused silica capillary interface. (f, g) Schematic illustrations of ion transfer mechanisms: hemispherical diffusion (aqueous → organic) and linear diffusion (organic → aqueous). (h) Cyclic voltammograms demonstrating concentration-dependent responses to heroin (1–50 μM) in the presence of common cutting agents (paracetamol and caffeine, 500 μM each), with characteristic peaks corresponding to heroin$^+$ transfer between phases. (i) Calibration curves showing excellent linearity ($R^2 > 0.99$) for anodic and cathodic peak currents. (j) Analytical validation demonstrating reproducible quantification of heroin across different expected concentrations and operators. This miniaturized platform makes selective, low-volume detection of heroin possible in complex matrices with minimal sample preparation. Reproduced with permission from a previous report [14]. Copyright 2022 Springer Nature.

performance of the system [10,26]. A novel method of heroin detection using a μLLI and a 3D-printed miniature platform is shown in Fig. 5. This device contains a fused silica capillary interface with a 25-μm diameter and specific electrodes—Ag/AgCl for the aqueous phase and Ag/AgTPBCl for the organic phase. Even with high concentrations (500 μM) of typical cutting agents, the platform can detect heroin selectively by taking advantage of ion transfer mechanisms between immiscible electrolyte solutions. With only microliter volumes required, the compact design is suitable for forensic sample analysis and offers outstanding consistency across several operators. Nanocomposites containing metallic nanoparticles, graphene, and carbon nanotubes are recent developments in electrode materials that greatly increase the surface area and catalytic efficiency. These improvements are gradually resolving major issues in field detection, such as system component contamination and electrode fouling [14,27].

## 4. DETECTION METHODS AND APPLICATIONS

### 4.1 Portable Drug Detection Systems

The extent of narcotics abuses and the numbers of overdoses and trafficking incidents have persistently increased in past decades [28,29]. Therefore, the development of accurate, field-deployable drug detection systems is essential. Fig. 6 (a) shows a trained drug detection dog inspecting a suitcase for illicit substances, representing a traditional drug detection method. Fig. 6 (b) shows a portable electronic drug detection device applied

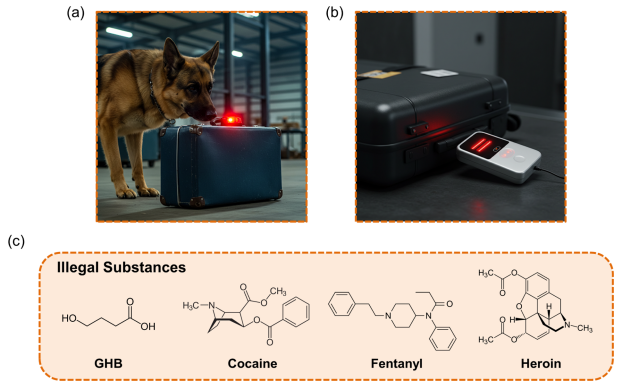


**Fig. 6.** Conventional and modern approaches for illicit drug detection and representative chemical structures. (a) Trained detection dog inspecting a suitcase for illicit substances, representing traditional drug detection methods. (b) Portable electronic drug detection device applied to a suitcase, displaying modern field-deployable technologies for rapid and noninvasive drug screening. (c) Chemical structures of commonly abused substances, including GHB, cocaine, fentanyl, and heroin.

to a suitcase, displaying modern field-deployable technologies for rapid and noninvasive drug screening. While the traditional drug detection method remains valuable, electronic sensing platforms address numerous persistent shortcomings, including consistency and repeatability, lifetime cost, quantification ability, and portability. Some commonly abused substances are GHB, cocaine, fentanyl, and heroin, as shown in Fig. 6 (c). Recently, researchers have used numerous approaches to develop a portable drug detection system for rapid, on-site use.

Li et al. developed a compact digital linear ion trap mass spectrometer that combines a membrane desorption sampling head with a separate-region corona discharge ionization (CDI) source for reagent-free, field-deployable drug detection [30]. A 25-μm semipermeable polydimethylsiloxane membrane selectively transmits volatile and semivolatile drug molecules while blocking particulates. Rapid thermal desorption then strips nonvolatile residues, suppressing matrix effects. The miniaturized digital ion trap completes full-scan and tandem mass spectrometry cycles in less than 10 s. In benchmark trials, the system correctly identified 18 widely trafficked drugs, including cocaine, methamphetamine, ketamine, fentanyl analogs, and several synthetic cannabinoids. Using cocaine as a model, the system achieved a dynamic range of more than two orders of magnitude and a 10-pg limit of detection, meeting roadside and customs cutoffs for drug detection. A built-in spectral library workflow automatically matches full-scan spectra and validates the results with collision-induced dissociation product ion spectra that mirror laboratory systems, providing ease of use and making extension to new analytes possible. The practical applicability of the system was demonstrated using an unknown seized sample. The system correctly identified the sample as synthetic marijuana AB-PINACA and ADB-BUTINACA. By tight integration of membrane sampling, reagent-free CDI, and digital ion trap, the system exhibits high specificity, sub-10-s analysis, and automated data interpretation, making possible a wide range of applications, including roadside checks, customs inspections, and rapid forensic triage [31,32].

### 4.2 Drug Analysis in Complex Samples

Because the sensing ability in a complex sample is an essential factor to consider for the practical use of drug detection systems, many studies not only focus on the sensing ability of target substances but also consider the potential interference caused by common contaminations occurring in real-life samples. Studies mentioned previously in this review, including the detection of GHB, heroin, fentanyl, and cocaine, explored the ability to prevent interference from potential contaminants. Because GHB is mostly abused by adding it to alcoholic beverages, in the work done by Zhang et al., the ability of the system to detect GHB in beer, vodka, whisky, soju, tequila, Chinese spirits, and brandy was examined [5,6]. In addition, because street-level narcotics have a high potential for contamination by multiple cutting agents, the heroin sensor developed by Borgul et al. and the fentanyl sensor developed by Goodchild et al. were tested for their ability to detect the target substance in the presence of common cutting agents, such as caffeine, glucose, acetaminophen, and theophylline [10,14]. Furthermore, the microfluidic electrochemical aptamer-based cocaine sensor built by Swensen et al. was developed for real-time monitoring of cocaine in undiluted blood serum [7]. While the systems developed in these studies have all shown excellent sensing abilities in the presence of potential interference, in this section, further elaboration on drug detection in complex samples is provided by examining specific studies on the topic.

Nguyen et al. developed a battery-powered portable capillary-electrophoresis platform with capacitively coupled contactless conductivity detection that delivers low-cost, on-site screening of amphetamine-type stimulants in the forms of street-grade tablets and biological fluids [33]. The instrument couples a capillary to a miniaturized high-voltage module and an in-house headstage, all driven by a 12-V lithium-ion battery. By operating in an arginine/acetate electrolyte that suppresses electro-osmotic drift, the system baseline-resolves methamphetamine, MDMA, MDA, and MDEA and quantifies them over four orders of magnitude. Detection limits reach 0.5 ppm for direct injections and 10 ppb after a 50-fold ethyl-acetate preconcentration step, matching the roadside and workplace

testing cutoffs. In field trials, the system correctly detected methamphetamine in street-grade pills and correctly identified methamphetamine and MDMA users from pretreated urine samples of suspects. Confirmation of the result was done using gas chromatography mass spectrometry, yielding a correlation coefficient for the two data of more than 0.99. Matrix interferents, such as caffeine, paracetamol, and inorganic cations, caused negligible interference, and carry-over was eliminated by a simple buffer flush, making fully reagent-free operation possible. Overall, the system exhibited high selectivity, parts-per-billion sensitivity, and dual-matrix compatibility for accurate on-site screening of complex samples of illicit substances.

Peng et al. developed a surface-enhanced Raman spectroscopy (SERS) kit that merges rapid hair pretreatment with gap mode Au-nanocake (Au NC) amplifiers to achieve 5 min on-site methamphetamine detection in hair [34]. After a brief acetone wash to remove surface impurities, hair solubilization under alkaline conditions releases methamphetamine embedded in the hair matrix. Methamphetamine can then be extracted from hair through liquid–liquid microextraction. Mixing the extract with Au NCs and sodium chloride induces stacking that provides hotspots, selectively amplifying the 993- and 1200-$cm^{-1}$ fingerprints of methamphetamine. The handheld Raman module then rapidly acquires spectra, exhibiting a 0.5-ppb limit of detection in standards, semiquantification across 0.5–160 ppb, and clear identification of 8 ppb in spiked hair, meeting the forensic cutoff. Coupling the matrix removal method with nanogap SERS made it possible to detect methamphetamine in hair accurately with high sensitivity and specificity.

## 5. CONCLUSIONS

Recent progress in drug sensor technology has made possible the rapid, sensitive, and selective detection of major illicit substances, such as GHB, cocaine, fentanyl, and heroin. By integrating optical and electrochemical transduction mechanisms with advanced materials, including molecularly imprinted polymers, aptamers, and ionic liquid-modified electrodes, modern sensors have demonstrated robust performance, even in complex, real-world matrices. The development of portable and miniaturized platforms, such as smartphone-integrated potentiostats and 3D-printed microfluidic devices, bridges the gap between laboratory-grade precision and field applicability, facilitating on-site analysis for law enforcement, clinical diagnostics, and public health interventions. Despite these advances, persistent challenges remain, such as mitigating matrix effects, improving long-term operational stability, and achieving reliable detection under diverse and uncontrolled conditions. To address these limitations, the integration of advanced data processing, particularly ML, is becoming increasingly essential. ML algorithms can enhance pattern recognition, compensate for sensor drift, and improve analyte discrimination in complex mixtures, thereby complementing physical sensor engineering. In this context, recent work on chemoresistive sensor arrays based on 2D materials demonstrates the high potential of electronic nose platforms for narcotics detection, where resistance change patterns from multichannel sensor arrays are analyzed using ML to achieve high accuracy and selectivity [35-38]. In conclusion, the convergence of innovative materials, device engineering, portable systems, and ML-driven data analytics is poised to transform illicit drug detection, supporting more-effective monitoring, prevention, and intervention strategies worldwide.

### CRediT Authorship Contribution Statement

**Hyuk Jin Kim:** Investigation, Data curation, Methodology, Visualization, Writing—original draft, Writing—review and editing. **Jun Uh Hyun:** Investigation, Data curation, Methodology, Visualization, Writing—original draft, Writing—review and editing. **Ho Won Jang:** Conceptualization, Project administration, Supervision, Writing—review and editing.

### Declaration of Competing Interest

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

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