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REVIEW

Digital droplets: AI in real-time monitoring of substance abuse – a review

C. Indhu Malar[1*†], Preetha Elizabeth Chaly[1†], Deepa Sundareswaran[2†] and Akila Ganesh[3†]

[1]Department of Public Health Dentistry, Meenakshi Ammal Dental College and Hospital, Meenakshi Academy of Higher Education and Research (Deemed to be University), Chennai, India
[2]Faculty of Occupational Therapy, Meenakshi Academy of Higher Education and Research (Deemed to be University), Chennai, India
[3]Department of Public Health Dentistry, Sri Ramachandra Dental College and Hospital, Sri Ramachandra Institute of Higher Education and Research, Chennai, India

*__Correspondence:__
C. Indhu Malar
drindhu.phd@madch.edu.in

†__ORCID:__
C. Indhu Malar
0000-0001-7085-8297
Preetha Elizabeth Chaly
0000-0003-2922-5097
Deepa Sundareswaran
0009-0009-7438-4290
Akila Ganesh
0000-0003-1557-8000

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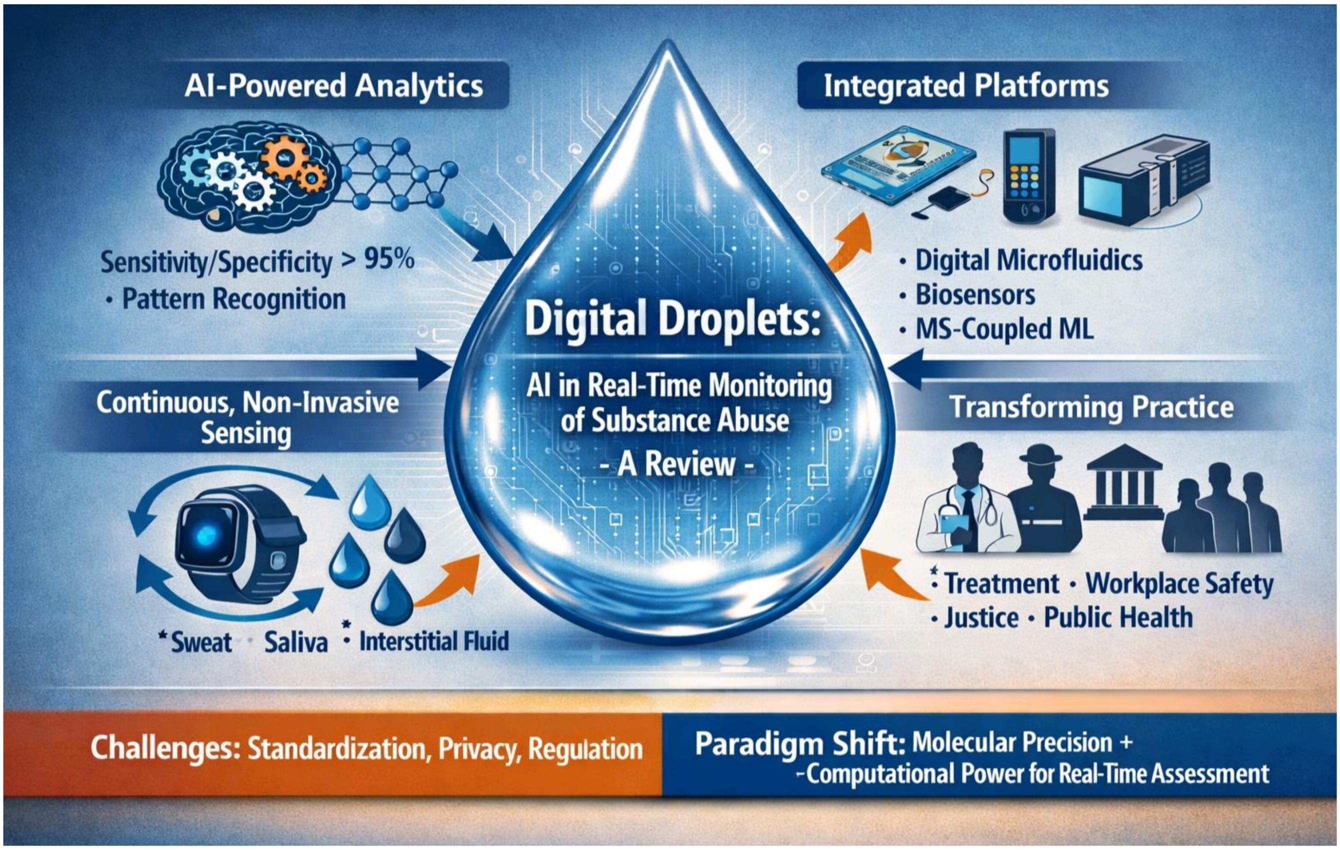
Substance abuse affects over 275 million people globally, demanding innovative detection strategies beyond conventional drug testing limitations. This review examines AI-powered analytical platforms integrated with liquid biopsy technologies, termed "digital droplets," for real-time substance abuse monitoring. We systematically analysed advances in AI-enhanced platforms including digital microfluidics, biosensor integration, mass spectrometry-coupled machine learning, and wearable monitoring devices from studies published between 2018 and 2025. AI algorithms demonstrate remarkable capabilities in pattern recognition and multiplexed analyte detection, with deep learning models achieving sensitivity and specificity exceeding 95% in identifying poly-drug use patterns. Digital droplet platforms with convolutional neural networks enable real-time signal processing, reducing detection time from hours to minutes. Wearable biosensors with edge computing facilitate continuous monitoring through non-invasive sampling of sweat, interstitial fluid, and saliva, while predictive models identify relapse risk patterns by integrating longitudinal exposure data with behavioural covariates. These technologies address critical limitations including delayed turnaround times and limited throughput, with applications spanning addiction treatment monitoring, workplace safety, criminal justice supervision, emergency medicine, and precision medicine approaches. Significant challenges persist including standardization across diverse populations, regulatory framework development, data privacy concerns, and ensuring equitable access. Digital droplets represent a paradigm shift in substance abuse monitoring, merging molecular precision with computational power to enable real-time, objective assessment of drug exposure, offering unprecedented opportunities for personalized intervention, treatment optimization, and public health surveillance.

Keywords: digital droplets, artificial intelligence, substance abuse, liquid biopsy, real-time monitoring, deep learning, biosensors

Graphical abstract



Introduction

Substance abuse disorders affect over 275 million people globally, contributing to significant morbidity, mortality, and socioeconomic burden (1). Traditional drug testing methods, including immunoassays and chromatography-mass spectrometry, while accurate, suffer from inherent limitations such as delayed turnaround times, requirement for specialized laboratory infrastructure, and inability to provide continuous monitoring (2). The advent of liquid biopsy technologies combined with artificial intelligence has catalysed a paradigm shift in substance abuse detection, enabling real-time, minimally invasive monitoring through analysis of biological fluids such as blood, urine, saliva, sweat, and interstitial fluid (3).

The term "digital droplets" encompasses a convergence of microfluidic technologies, biosensor platforms, and computational intelligence that transforms minute biological samples into rich datasets amenable to sophisticated algorithmic analysis (4). This integration addresses several critical gaps in current substance abuse monitoring: the need for rapid point-of-care detection, continuous surveillance in community settings, identification of poly-drug use patterns, and prediction of relapse risk through longitudinal data analysis (5). The application of machine learning and deep learning algorithms to liquid biopsy data enables pattern recognition capabilities that exceed human analytical capacity, facilitating detection of complex drug metabolite profiles and temporal usage patterns (6).

This review synthesizes recent advances in AI-enhanced liquid biopsy technologies for substance abuse monitoring, examining the technical foundations, clinical applications, and translational challenges of digital droplet platforms. We explore how these innovations are reshaping addiction medicine, forensic toxicology, and public health surveillance while considering the ethical and regulatory dimensions of implementing these technologies in diverse populations and settings.

Technological foundations of digital droplets

Liquid biopsy technologies

Liquid biopsy refers to the analysis of biological fluids to detect biomarkers of disease or exposure, offering advantages over traditional tissue sampling including minimal invasiveness, serial sampling capability, and accessibility (7). In substance abuse monitoring, liquid biopsies encompass various matrices: blood plasma for quantitative pharmacokinetic profiling, urine for detection of parent drugs and metabolites with extended detection windows, oral fluid for recent use determination, sweat for continuous non-invasive monitoring, and interstitial fluid accessed through microneedle arrays for real-time transdermal sensing (8).

Digital microfluidics has emerged as a cornerstone technology, enabling precise manipulation of microliter to nanolitre sample volumes through electrowetting on dielectric surfaces (9). These platforms integrate sample preparation, analyte concentration, and detection in miniaturized formats compatible with point-of-care deployment. Droplet-based microfluidics allows compartmentalization of individual reactions, enabling high-throughput screening and multiplexed detection of multiple substances simultaneously within a single sample (10).

Biosensor integration

Electrochemical biosensors represent a dominant platform for substance abuse detection due to their rapid response times, sensitivity, and compatibility with miniaturization (11). These sensors employ recognition elements such as aptamers, molecularly imprinted polymers, or antibodies that bind specifically to target drugs or metabolites, generating measurable electrical signals upon binding events. Surface-enhanced Raman spectroscopy biosensors provide molecular fingerprinting capabilities, enabling simultaneous detection of multiple drugs through spectral pattern analysis (12).

Optical biosensors utilizing fluorescence resonance energy transfer, surface plasmon resonance, or colorimetric detection offer label-free, real-time monitoring capabilities (13). Recent innovations include paper-based microfluidic biosensors that combine low cost with portable functionality, particularly valuable for resource-limited settings and field applications. The integration of nanomaterials—including gold nanoparticles, carbon nanotubes, and quantum dots—enhances sensitivity and expands the dynamic range of detection, enabling quantification of drugs at clinically relevant concentrations (14).

Mass spectrometry platforms

Mass spectrometry remains the gold standard for substance identification and quantification due to its unparalleled specificity and sensitivity (15). Miniaturized mass spectrometry systems, including ambient ionization techniques such as paper spray ionization and direct analysis in real time, enable rapid analysis without extensive sample preparation. These platforms generate complex spectral data requiring sophisticated computational analysis to extract meaningful information regarding substance identity, concentration, and metabolite profiles (16).

Wearable monitoring devices

Wearable biosensors represent a transformative approach to continuous substance abuse monitoring in naturalistic settings (17). These devices employ microneedle arrays, iontophoretic sampling, or passive diffusion to access sweat or interstitial fluid, analysing biomarkers of recent drug exposure. Integration of flexible electronics, wireless data transmission, and miniaturized power sources enables unobtrusive monitoring over extended periods. Wearable platforms demonstrate particular promise for monitoring treatment adherence, detecting early relapse indicators, and providing objective data to inform clinical decision-making (18).

Artificial intelligence architectures for substance abuse detection

Machine learning approaches

Traditional machine learning algorithms including support vector machines, random forests, and gradient boosting methods have demonstrated efficacy in classifying drug exposure status from biosensor data (19). These algorithms excel at handling structured, tabular data such as electrochemical sensor outputs, spectral features, or temporal concentration profiles. Feature engineering—the process of selecting and transforming raw sensor data into informative inputs—represents a critical step determining algorithm performance. Machine learning models enable real-time classification of drug presence, estimation of concentration levels, and identification of poly-drug use patterns from multiplexed sensor arrays (20).

Deep learning architectures

Deep learning has revolutionized pattern recognition in complex, high-dimensional data characteristic of liquid biopsy analyses (21). Convolutional neural networks excel at processing spectral data from mass spectrometry or Raman spectroscopy, automatically learning hierarchical feature representations that capture subtle patterns indicative of specific substances or metabolites. Recurrent neural networks and long short-term memory architectures enable analysis of temporal sequences, critical for modelling pharmacokinetic profiles and predicting drug elimination kinetics from continuous monitoring data (22).

Autoencoders facilitate dimensionality reduction and anomaly detection, identifying unusual patterns that may indicate novel psychoactive substances or drug adulteration (23). Transfer learning approaches leverage models pre-trained on large spectroscopic or chromatographic databases, reducing the data requirements for training substance-specific detection algorithms. Ensemble methods combining multiple deep learning architectures achieve state-of-the-art performance, with reported sensitivities and specificities exceeding 95% for major drug classes including opioids, stimulants, cannabinoids, and benzodiazepines (24).

Edge computing and real-time processing

Edge computing architectures deploy AI algorithms directly on wearable devices or point-of-care platforms, enabling real-time data processing without cloud connectivity requirements (25). This approach addresses latency concerns, preserves data privacy by minimizing transmission of sensitive health information, and enables immediate alerts when substance exposure is detected. Optimization techniques including model quantization, pruning, and knowledge distillation reduce computational requirements, allowing sophisticated deep learning models to operate on resource-constrained devices (26).

Predictive analytics and relapse risk modelling

Beyond detection, AI algorithms enable predictive modelling of relapse risk by integrating longitudinal substance exposure data with behavioural, environmental, and physiological covariates (27). Time-series forecasting models identify patterns preceding relapse events, enabling pre-emptive interventions. Natural language processing algorithms analyse clinical notes, patient-reported outcomes, and electronic health records to extract risk factors and protective elements, integrating these with objective biomarker data to generate comprehensive risk assessments (28).

Clinical and forensic applications

Addiction treatment monitoring

Digital droplet technologies address a fundamental challenge in addiction treatment: objective verification of abstinence and early detection of substance use (29). Continuous monitoring through wearable biosensors provides clinicians with real-time data to inform treatment modifications, while reducing the burden and stigma associated with frequent clinic visits for supervised urine testing. AI-powered predictive models identify high-risk periods, enabling targeted deployment of behavioural interventions or medication adjustments. Integration with smartphone applications and telemedicine platforms creates comprehensive monitoring ecosystems supporting recovery (30).

Emergency medicine and critical care

In emergency departments, rapid substance identification is crucial for appropriate clinical management of intoxication, overdose, and poly-drug exposure (31). Point-of-care digital droplet platforms provide results within minutes, guiding resuscitation strategies, antidote administration, and disposition decisions. AI algorithms trained on extensive toxicology databases assist in identifying novel psychoactive substances and predicting clinical trajectories based on detected drug profiles. These capabilities are particularly valuable amid the evolving landscape of synthetic opioids, designer stimulants, and other emerging substances (32).

Workplace safety and transportation

Safety-sensitive industries including transportation, construction, and manufacturing require effective drug testing programs to mitigate accident risk (33). Digital droplet technologies enable rapid, on-site testing with results available before shift commencement. Non-invasive sampling through oral fluid or sweat reduces collection privacy concerns and adulteration potential compared to urine testing. AI-powered interpretation accounts for factors affecting drug detection windows, providing nuanced assessments of impairment risk rather than binary positive/negative results (34).

Criminal justice and forensic applications

Community supervision of individuals with substance use conditions constitutes a major application domain for continuous monitoring technologies (35). Wearable biosensors provide objective compliance data for drug court participants, probationers, and parolees, potentially reducing incarceration while ensuring accountability. Forensic toxicology laboratories employ AI-enhanced mass spectrometry platforms for comprehensive drug screening in death investigations, driving under the influence cases, and drug-facilitated crimes. Machine learning algorithms accelerate analysis of backlogged cases while improving detection of uncommon substances (36).

Public health surveillance

Population-level monitoring through aggregated, de-identified data from digital droplet platforms enables real-time surveillance of substance use trends (37). Early detection of emerging drug threats, identification of geographic hotspots, and characterization of poly-drug use patterns inform public health responses. Integration with syndromic surveillance systems tracking overdose presentations, infectious disease complications, and treatment admissions creates comprehensive epidemiological intelligence supporting prevention efforts and resource allocation (38).

Performance characteristics and validation

Analytical validation of digital droplet platforms requires demonstration of sensitivity, specificity, precision, accuracy, and robustness across relevant concentration ranges and sample matrices (39). Studies report detection limits in the nanogram per millilitre to picogram per millilitre range for major drug classes, with linear dynamic ranges spanning three to four orders of magnitude. Cross-reactivity assessments evaluate specificity against structurally similar compounds, common medications, and endogenous interferents (40).

Clinical validation examines concordance with reference laboratory methods, typically gas chromatography-mass spectrometry or liquid chromatography-tandem mass spectrometry (41). Meta-analyses of AI-enhanced detection platforms demonstrate pooled sensitivities of 92-97% and specificities of 94-98% compared to confirmatory testing. However, performance varies by drug class, matrix, and time since use, necessitating substance-specific validation studies (42).

External validation using diverse populations represents a critical requirement given known variations in drug metabolism influenced by genetic polymorphisms, age, sex, body composition, and co-exposures (43). Algorithmic fairness assessments evaluate whether AI models exhibit differential performance across demographic groups, addressing concerns regarding equitable application of these technologies. Prospective validation in real-world settings establishes clinical utility and implementation feasibility beyond controlled laboratory conditions (44).

Challenges and limitations

Technical challenges

Matrix effects, wherein endogenous compounds in biological fluids interfere with analyte detection, represent a persistent challenge requiring robust sample preparation and algorithmic compensation (45). Temperature variations, humidity, and other environmental factors affect sensor performance, particularly for wearable devices deployed in uncontrolled conditions. Battery limitations constrain continuous operation of wearable platforms, necessitating power-efficient sensor designs and data transmission protocols (46).

Regulatory and standardization issues

Regulatory pathways for AI-enabled diagnostic devices remain evolving, creating uncertainty regarding approval requirements and clinical implementation (47). Lack of standardized calibrators, quality control materials, and proficiency testing programs for emerging substances complicates validation and inter-laboratory comparisons. Harmonization of cutoff concentrations for defining positive results across different platforms and jurisdictions represents an ongoing challenge (48).

Data privacy and security

Continuous monitoring generates extensive personal health data requiring robust privacy protections (49). Cybersecurity vulnerabilities in connected devices and cloud platforms create risks of unauthorized access or data breaches. Balancing the need for data sharing to support public health surveillance with individual privacy rights requires careful policy development. Questions regarding data ownership, secondary use permissions, and retention periods remain contested (50).

Ethical considerations

Mandatory monitoring in employment, criminal justice, or child welfare contexts raises concerns regarding autonomy, consent, and potential discrimination (51). The risk of false positives leading to adverse consequences—including loss of employment, custody disputes, or incarceration—demands high performance standards and confirmatory testing protocols. Ensuring equitable access to these technologies across socioeconomic strata and avoiding exacerbation of health disparities requires deliberate policy interventions (52).

Algorithmic limitations

AI models trained on limited or biased datasets may not generalize to diverse populations or novel drug formulations (53). The black-box nature of complex deep learning models complicates interpretation and may reduce clinical acceptance. Adversarial vulnerabilities, wherein deliberate perturbations fool algorithms, represent security concerns in high-stakes applications. Continuous model updating to accommodate emerging substances and evolving use patterns requires robust data pipelines and revalidation protocols (54).

Future directions

Advances in nanotechnology promise increasingly sensitive and miniaturized sensors capable of detecting substances at trace concentrations in minimally invasive samples (55). Integration of multi-omics approaches—combining metabolomics, proteomics, and transcriptomics—may enable comprehensive characterization of substance abuse effects beyond simple presence/absence determination. Quantum computing applications to molecular simulation and pattern recognition could accelerate drug identification and metabolite prediction (56).

Federated learning architectures enable collaborative model training across multiple institutions without centralizing sensitive data, addressing privacy concerns while leveraging large datasets (57). Explainable AI methods will enhance clinical interpretability by providing human-understandable rationales for algorithmic decisions. Integration with digital therapeutics platforms creates closed-loop systems where objective monitoring data directly informs adaptive interventions (58).

Expansion beyond traditional drugs of abuse to monitor medication adherence for addiction pharmacotherapy, such as buprenorphine or naltrexone, represents a valuable application domain (59). Environmental monitoring of wastewater and air samples using AI-enhanced platforms could provide community-level substance use surveillance without individual identification. Ultimately, personalized medicine approaches leveraging pharmacogenomic data integrated with real-time monitoring may optimize treatment selection and dosing for substance use disorders (60).

Conclusion

Digital droplets represent a convergence of liquid biopsy technologies and artificial intelligence that fundamentally transforms substance abuse monitoring. These platforms address critical limitations of conventional drug testing through rapid turnaround times, continuous surveillance capabilities, multiplexed detection, and predictive analytics. AI algorithms demonstrate exceptional performance in pattern recognition, achieving sensitivities and specificities approaching or exceeding traditional laboratory methods while enabling real-time decision support.

Applications span the continuum from individual patient care in addiction treatment through population health surveillance, with demonstrated utility in emergency medicine, workplace safety, criminal justice, and forensic contexts. The integration of wearable biosensors with edge computing enables unobtrusive monitoring in naturalistic settings, providing objective data to inform personalized interventions and support sustained recovery.

Significant challenges remain, including technical limitations requiring continued innovation, regulatory uncertainty demanding policy development, privacy concerns necessitating robust protections, and ethical considerations requiring careful deliberation. Ensuring equitable access and avoiding algorithmic bias represent critical priorities as these technologies transition from research to widespread implementation.

The digital droplet paradigm exemplifies precision medicine principles applied to substance use disorders, enabling objective, individualized assessment and intervention. As these technologies mature and evidence of clinical utility accumulates, they hold promise to reduce the substantial morbidity, mortality, and societal costs associated with substance abuse while respecting individual dignity and autonomy. The successful integration of molecular precision with computational intelligence offers unprecedented opportunities to transform substance abuse monitoring from episodic, reactive testing to continuous, proactive surveillance supporting prevention, treatment, and recovery across diverse populations and settings.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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