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Publication Date
2019-10-01

DOI
10.1016/j.snb.2019.04.053

Peer reviewed

Wearable electrochemical glove-based sensor for rapid and on-site detection of fentanyl

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Abstract

Rapid, on-site detection of fentanyl is of critical importance, as it is an extremely potent synthetic opioid that is prone to abuse. Here we describe a wearable glove-based sensor that can detect fentanyl electrochemically on the fingertips towards decentralized testing for opioids. The glove-based sensor consists of flexible screen-printed carbon electrodes modified with a mixture of multiwalled carbon nanotubes and a room temperature ionic liquid, 4-(3-butyl-1-imidazolio)-1-butanesulfonate). The sensor shows direct oxidation of fentanyl in both liquid and powder forms with a detection limit of 10 μM using square-wave voltammetry. The "Lab-on-a-Glove" sensors, combined with a portable electrochemical analyzer, provide wireless transmission of the measured data to a smartphone or tablet for further analysis. The integrated sampling and sensing methodology on the thumb and index fingers, respectively, enables rapid screening of fentanyl in the presence of a mixture of cutting agents and offers considerable promise for timely point-of-need screening for first responders. Such a glove-based "swipe, scan, sense, and alert" strategy brings chemical analytics directly to the user's fingertips and opens new possibilities for detecting substances of abuse in emergency situations.

Graphical abstract

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*Corresponding authors: drewhall@ucsd.edu (D. A. Hall) and josephwang@ucsd.edu (J. Wang).
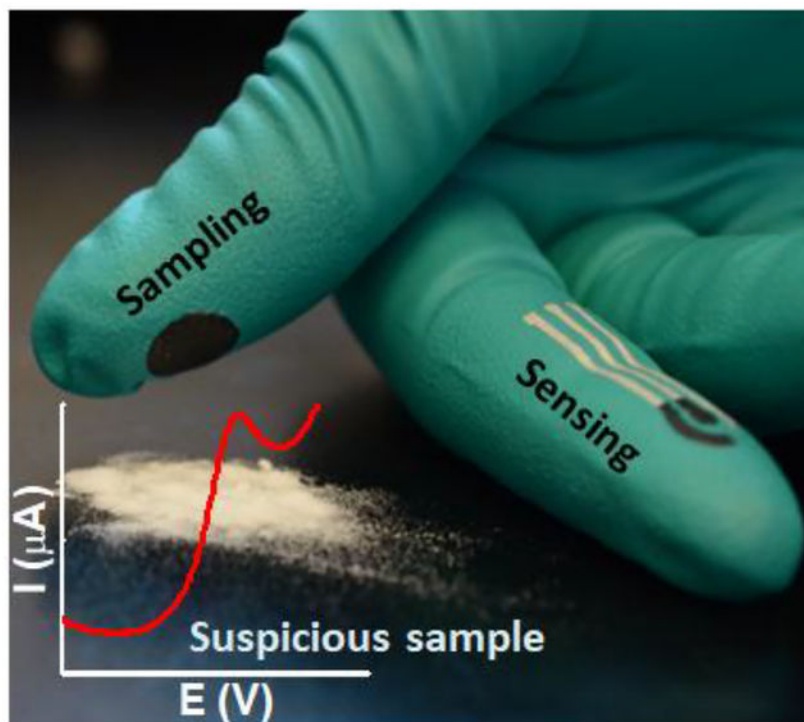[1]Authors with equal contributions
[2]Authors with equal correspondence

Author Contributions
A.B and R.K.M contributed equally to this work. All authors have contributed to the manuscript and have given approval to the final version of the manuscript.

The authors declare no competing financial interest.

Keywords

Fentanyl; Glove based-sensor; Opioids; On-site drug screening; Electrochemical sensors

1. Introduction

Wearable sensors are well positioned to revolutionize healthcare monitoring through seamless integration in our daily routines [1–3]. For example, wearable biosensing has been demonstrated with microneedles [4–7], epidermal microfluidics [8–11], and mouthguard-based sensor platforms [12] for continuous monitoring of electrolytes and metabolites. Other examples of cutting-edge wearable devices include tattoo sensors for non-invasive analysis of biomarkers, such as alcohol [13], glucose [14,15], and lactate [16] in epidermal biofluids (ISF and sweat). Glove-based sensors have been shown for detection of environmental and security threats of organophosphates [17], explosives and gunshot residues [18]. Incorporating chemical sensors into wearable platforms (e.g., gloves, microfluidics, tattoos, etc.) offer the supremacy of lab-centered chemical analysis in a convenient form that can be measured anywhere [19].

While most early wearable sensors to date have focused on fitness, wellness, and healthcare, there are tremendous opportunities for security and forensic applications of these devices [20,21] and towards monitoring drugs of abuse [22,23]. Drug abuse and misuse have increased significantly in recent years and is a rapidly growing and major problem for our society with tremendous costs (>$400 billion annually) due to lost productivity, health care needs, and legal processes [24]. Specifically, the misuse of prescription pain medications has

become a public health epidemic, including the diversion of prescribed medications, such as oxycodone, buprenorphine, morphine, and fentanyl [25].

Fentanyl is a sedative and a Schedule II drug under the controlled substance act. It is currently being used as an analgesic and anesthetic. It is 50 to 100× more potent than morphine and 30 to 50× more potent than heroin. Fentanyl has been progressively used as an adulterant in illegitimate substances, such as heroin [26]. In 2015, the Drug Enforcement Agency issued a nationwide alert calling fentanyl a "threat to health and public safety." Moreover, recently the Centers for Disease Control and Prevention reported that fentanyl and associated analogues were connected with over half of the opioid overdoses in ten states during the second half of 2016 [27]. Opioids represent a grave threat to public health and safety, in particular to first responders trying to treat people who have overdosed. Even small amounts of opioids present can become aerosolized and toxic. Thus, identification of fentanyl in trace quantities is crucial to deal with the current widespread epidemic.

Currently, liquid chromatography (LC) with mass spectrometry (MS) and immunoassay techniques are the gold standard for fentanyl detection and quantification [28,29]. Recent advanced technologies include surface enhanced Raman spectroscopy (SERS), which offer sensitive detection of fentanyl in heroin samples with a limit of detection (LOD) of 100 ng/mL [30]. Electromembrane extraction coupled with voltammetric readout demonstrated detection of sufentanil (a fentanyl analogue) in urine and plasma samples, with an LOD of 2×10^{-8} mol/dm^{-3} [31]. Antibody-based biosensors, employing enzyme-linked immunosorbent assays (ELISAs) and automated homogeneous enzyme immunoassays have also shown potential applications for fentanyl detection with an LOD of 1 ng/mL [32]. However, these techniques all require laboratory-based instrumentation, as well as complex sample preparation and operations, precluding on-site detection by law enforcement officers or first responders. In this regard, electrochemical analysis provides a unique combination of high sensitivity, fast response, low cost, and ease of operation.

Herein, we report a wearable glove with flexible electrochemical sensors integrated on the fingertips for spot identification of illicit drugs, specifically fentanyl. This is the first demonstration of a wearable electrochemical opioid drug detection platform towards on-site fentanyl screening. Glove-based wearable sensors, capable of chemical sensing at the fingertips, have been developed recently for detecting gunshot residues and nerve-agent threats [17,18,33]. The new fentanyl glove detection device carries out the sampling and electrochemical sensing steps on different fingers, with the thumb finger used for collection of drug residues or powder samples along with the index finger (printed carbon electrodes coated with an ionic liquid/multiwall carbon nanotube composite film) for fentanyl sensing (Figure 1, A and B). Electrochemical (voltammetric) measurements were performed after completing the "electrochemical cell" by joining the thumb (sampling) and index (sensing) fingers. These measurements relied on square-wave voltammetric analysis, where the anodic peak current response, corresponding to direct fentanyl oxidation, is sent to a nearby tablet (or smartphone) via a Bluetooth wrist-worn potentiostat. The resulting glove-based sensor system thus enables rapid (~1 min) screening of fentanyl in both powder and liquid forms, bringing the power of centralized lab testing to the point-of-need. This allows first

responders to rapidly assess unknown suspicious powders in emergency situations and deliver appropriate care for the patient while taking necessary precautions themselves.

2. Experimental

2.1 Chemicals and reagents

Fentanyl (1.0 mg/mL in methanol, certified reference material), acetaminophen, glucose, caffeine, theophylline, multi-walled carbon nanotubes (MWCNT, O.D. × L 6–13 nm × 2.5–20 μm), polyethylenimine (PEI), the ionic liquid of 4-(3-Butyl-1-imidazolio)-1-butanesulfonate, xylene, dipotassium hydrogen phosphate (K_2HPO_4), potassium dihydrogen phosphate (KH_2PO_4), sodium acetate, potassium chloride, and agarose were all purchased from Sigma-Aldrich (MO, USA). Carbon and Ag/AgCl inks (Ercon, Inc., Wareham, MA) were used to print the sensors on green nitrile powder-free exam gloves purchased from Kimberly-Clark (Roswell, GA). Deionized water was used to prepare aqueous electrolyte solutions. All solvents and chemicals were of analytical grade and used without further purification.

2.2 Glove-based sensor fabrication

Fabrication of the disposable glove-based sensor was carried out utilizing a semiautomatic MPM-SPM screen printer (Speedline Technologies, Franklin, MA). A 125 μm thick stainless-steel stencil (Metal Etch Services, San Marcos, CA) was designed using AutoCAD and laser-cut. To facilitate a smooth and planar printing surface, a finger mold ($10.0 \times 2.3 \times 1.3$ cm^3) was drawn using SolidWorks 3D CAD (DS SolidWorks, Waltham, MA) and printed using a Mojo 3D printer (Stratasys, Eden Prairie, MN). The 3D printed molds were inserted into the nitrile gloves before screen-printing the sensor structures. The Ag/AgCl layer was printed on the index finger as the reference electrode and as a connecting pad, followed by a layer of carbon and an insulator layer to complete the sensing electrode. The screen-printed sensor was cured at 70°C for 10 min after each layer was printed. The Ag/AgCl-based ink served as the reference electrode, whereas carbon ink was used for the working and counter electrodes. The transparent insulating layer was carefully printed on the sensor interconnects to provide a dielectric segregation of the three-electrode system and to subside sensors short-circuits. (Reviewer 2, comment#3) The same printing procedure was used to print a circular carbon pad (1 cm diameter) on the thumb finger.

2.3 Preparation of the ionic liquid modified glove-based sensors

Multiwall carbon nanotubes (MWCNT) were added to an ethanol solution and sonicated for 1 h. Then, 2 mg (Reviewer 2, comment#3) IL, 4-(3-Butyl-1-imidazolio)-1-butanesulfonate, and PEI were added into the MWCNT organic phase solution and stirred for 2 h. The resulting solution was centrifuged to remove any unbound MWCNT, IL, and PEI in solution, resulting in the MWCNT-PEI-IL composite nanomaterial. Later, from the prepared nanomaterial (MWCNT-PEI composite (1:16 w/w ratio) and IL), a 10 mg sample was taken and dissolved in 50 μL of DI H_2O. The mixture was sonicated for 1 min. The developed composition was further diluted 6× in DI water and a final volume of 1.5 μL was drop-casted on the working electrode of the glove-based sensor. Each electrode was allowed to air dry for 10 minutes prior to use. For dry phase analysis, a semi-solid 1.0 wt % agarose gel was

prepared in a mixture of 0.1 M PBS and dispensed on the sensor (index finger) to cover the surface and provide a conductive medium for electrochemical analysis. The thickness of hydrogel was about 3 mm. Such hydrogel layer displayed high stability over 2 weeks upon storage of the gel-coated sensors in the refrigerator. It is significant to note that the glove sensor is designed for a single-use application, to avoid contamination from early testing. (Reviewer 1)

2.4 Electrochemical measurements

Electrochemical characterization was performed at room temperature using a PalmSens hand-held potentiostat (EmStat3 Blue with $10.0 \times 6.0 \times 3.4$ cm^3 dimensions, PalmSens, Houten, Netherlands) powered by a rechargeable Li–Po battery (Figure 1B). The PalmSens electrochemical analyzer can perform square wave voltammetry. The obtained data were wirelessly transmitted to a tablet to perform the analysis. The electrochemical sensing studies were performed by completing the "electrochemical cell" by joining the thumb (sample collector) with the sensing (index) finger (covered with 1.0 wt % agarose gel) and recorded fentanyl oxidation by square wave voltammetry (SWV) with optimized parameters of 10 Hz frequency, 20 mV amplitude, and 3 mV step potential.

2.5 Powder fentanyl swiping and scanning

Before contaminating the target surfaces (glass slides) with fentanyl, they were first rinsed with absolute ethanol, distilled water, and finally dried using air flow. Subsequently, the glass slides (10×10 mm) were contaminated using a 5 μL aliquot of the fentanyl stock solution. The drop-casted fentanyl solution was dried to a residue through evaporation at room temperature for 3–4 h under a fume hood.

The glove-based sensors were worn for the sampling and detection steps and connected to an electrochemical analyzer. The fentanyl powder residues were collected by swiping contaminated glass slides using the thumb finger followed by subsequent fentanyl sensing performed by joining the collection and sensing (index) finger (covered with 200 μL of 1 wt % agarose gel). After completing the electrochemical cell by joining the two fingers, the operator waited 2 min to perform the analysis. It should be noted that, to avoid any cross-contamination, each glove sensor was fabricated for a single use.

Safety note: According to United States Drug Enforcement Administration (DEA), fentanyl is potentially lethal, even at levels as low as 0.25 mg [34]. Therefore, all experiments including sample preparation and measurements that involved fentanyl handling, were strictly conducted inside a fume hood along with wearing appropriate personal protective equipment (PPE) using a university approved handling protocol. To perform sample swiping (dried fentanyl solution on a glass slide), all preparations and experiments were performed in a sealed air bag-based glove box (4 gal-capacity). The complete setup was placed inside a fume hood with continuous air flow.

3.   Results and discussion

3.1   Fentanyl sensing in liquid form

The glove-based wearable platform for fentanyl screening is shown in Figure 1. The developed wearable sensor that combines the screen-printed glove sensors with a portable electrochemical analyzer (Figure 1C) enables on-site fentanyl sampling and screening (Figure 1D). The square wave voltammetry (SWV) technique exhibits a distinct electrochemical fingerprint for fentanyl based on its direct irreversible oxidation on the carbon sensing electrode modified with the room temperature ionic liquid composite (MWCNT-PEI-IL).

The performance of the glove-based sensor was first assessed towards fentanyl screening in the liquid phase using buffer solution. Changes in the fentanyl concentrations were used to evaluate the dynamic behavior of the sensor. Figure 2A shows square wave voltammograms of fentanyl in PBS (0.1 M, pH 7.4) on ionic liquid-modified sensors, upon increasing fentanyl concentrations over the range of 10 – 100 μM. These fentanyl levels result in a single and distinct oxidation peak at +0.65 V (*vs.* Ag/AgCl), which is attributed to the oxidation of the tertiary amine groups present in the fentanyl structure [31]. The resulting calibration curve (shown in Figure 2B) demonstrates good linearity ($R^2 = 0.992$) with an estimated detection limit (LOD) of 10 μM (RSD = 3.2%, n = 6). It should be mentioned that the elevated background signal observed when increasing the fentanyl concentration on Figure 2A could be due to the presence of methanol in the fentanyl samples. It is well known that ionic liquids improve electrochemical processes [35]; however, the 4-(3-Butyl-1-imidazolio)-1-butanesulfonate ionic liquid coating here is essential for the fentanyl detection. No distinguishable fentanyl signal was seen using bare carbon sensors without the ionic liquid modification.

3.2   Fentanyl sensing in a powder form

After establishing the glove sensor response in liquid phase, the analysis was further extended to powder/dry phase to perform real-time and in-field analysis of fentanyl (see related Safety Note in Experimental section). As mentioned in the experimental section, a conducting agarose hydrogel (200 μL of 1 wt %) that covers the sensing finger was used as an electrolyte for the electrochemical measurements. During the sampling of fentanyl residues (dried fentanyl on a glass slide), the collection finger with the printed circular carbon pad swiped the test surface. The presence of fentanyl was detected by joining the sensing and collection fingers where the conducting agarose gel completed the electrochemical cell. The resulting square wave voltammograms of fentanyl in powder samples are presented in Figure 2C. It can be seen that a clear background signal (black curve) is recorded for the glove sensor before fentanyl swiping. After collecting a fentanyl sample, a sharp and distinct peak at +0.76 V (*vs.* Ag/AgCl) is observed, demonstrating the fentanyl electrochemical oxidation (Figure 2C, red curve). Compared to the fentanyl oxidation peak of +0.65 V in liquid phase (Figure 2A), lower electrolyte concentration in the powder form slows the oxidation kinetics and therefore a higher oxidation potential is expected. The analytical operation is based on the abrasive voltammetry technique (transfer of trace amounts of solid sample onto the surface of an electrode [36]) to rapidly identify the

presence of the drug. Faraday's law that predicts that ultra-small amounts of collected electroactive materials can give rise to significant (µA) currents, thus sampling of trace amounts of a solid material onto the electrode surface is sufficient for analysis (Reviewer 2, comment #1).

As a control, Figure 2D also illustrates the swiping and screening in the absence of fentanyl powders and shows no detectable signal. The elevated signal is likely due to the applied pressure while joining the figures, but there are no oxidation peaks present in the signal.

3.3 Electrochemical screening of fentanyl mixed with common cutting agents

Street drugs usually contain cutting agents or diluents. Thus, a sensitive and reliable sensor should be able to distinguish the target analyte signal in a heterogeneous sample. Common cutting agents acetaminophen, caffeine, glucose, and theophylline were selected to test the performance of the glove sensor. Figure 3 demonstrates the high selectivity of the sensor toward fentanyl in both liquid and powder forms (Figure 3D), along with the SWV response of different interferers. As shown in the measurements, only acetaminophen (Figure 3B) and theophylline (Figure 3F) undergo oxidation at around +0.12 V (*vs.* Ag/AgCl) and +0.80 V (*vs.* Ag/AgCl), respectively, which caused no interference for the fentanyl sensing.

Electrochemical sensing of fentanyl was performed in a mixture containing 100 µM of acetaminophen, caffeine and glucose in a liquid form (Figure 4A). A well-defined fentanyl oxidation peak at +0.63 V (*vs.* Ag/AgCl) along with a gradual increase in signal upon rising the fentanyl concentration from 10 to 100 µM was observed. The results show that these cutting agents do not introduce any drift or changes in the fentanyl peak, with results similar to the liquid-phase experiments presented in Figure 2A. Similarly, in the mixed powder form (Figure 4B), fentanyl oxidation showed a distinct peak around +0.72 V (*vs.* Ag/AgCl). These results demonstrate a highly selective glove-based sensor for fentanyl screening.

4. Conclusions

This work aimed at developing a glove-based wearable electrochemical sensor capable of detecting opioids. The concept was demonstrated by voltammetric detection of fentanyl in liquid and powder forms. The glove-based sensor was prepared by screen printing "sensing" and "sampling" fingers and coupling this with a wireless and portable electrochemical analyzer, suitable for on-site and one-touch sample-to-answer testing of suspicious samples. Our data demonstrate that the "Lab-on-a-Glove" sensor platform responds in a reproducible and selective manner and offers fentanyl detection in powder as well as in liquid samples in the range between 10 to 100 µM with a 10 µM LOD. Detection was also demonstrated in the presence of cutting agents with no interference. As such, the glove-based drug sensor addresses major challenges associated with reliable, rapid, on-site screening and field detection of opioids in connection to first responder safety, airport/border screening, or assessing medical facilities and potential terror threats. Further improvement in the peak identification can be achieved using our recently developed cyclic-square-wave voltammetric operation that yields distinct electrochemical fingerprint of fentanyl [37] (Reviewer 2, comment #1). Continued advances in electronics, particularly integration with

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miniaturized on-ring electrochemical systems, will further enhance such important field screening applications.

Acknowledgement

References

[1]. Matzeu G, Florea L, Diamond D, Advances in wearable chemical sensor design for monitoring biological fluids, Sensors Actuators B Chem 211 (2015) 403–418. doi:10.1016/j.snb.2015.01.077.

[2]. Bandodkar AJ, Wang J, Non-invasive wearable electrochemical sensors: a review, Trends Biotechnol 32 (2014) 363–371. doi:10.1016/j.tibtech.2014.04.005. [PubMed: 24853270]

[3]. Yang Y, Gao W, Wearable and flexible electronics for continuous molecular onitoring, Chem. Soc. Rev (2018). doi:10.1039/C7CS00730B.

[4]. Mishra RK, Vinu Mohan AM, Soto F, Chrostowski R, Wang J, A microneedle biosensor for minimally-invasive transdermal detection of nerve agents, Analyst 142 (2017) 918–924. doi:10.1039/C6AN02625G. [PubMed: 28220163]

[5]. V Mukerjee E, Collins SD, Isseroff RR, Smith RL, Microneedle array for transdermal biological fluid extraction and in situ analysis, Sensors Actuators A Phys 114 (2004) 267–275. doi:10.1016/j.sna.2003.11.008.

[6]. Mohan AMV, Windmiller JR, Mishra RK, Wang J, Continuous minimally-invasive alcohol monitoring using microneedle sensor arrays, Biosens. Bioelectron 91 (2017) 574–579. doi:10.1016/j.bios.2017.01.016. [PubMed: 28088750]

[7]. Bollella P, Sharma S, Cass AEG, Antiochia R, Microneedle-based biosensor for minimally-invasive lactate detection, Biosens. Bioelectron 123 (2019) 152–159. doi:10.1016/j.bios.2018.08.010. [PubMed: 30177422]

[8]. Gao W, Emaminejad S, Nyein HYY, Challa S, Chen K, Peck A, Fahad HM, Ota H, Shiraki H, Kiriya D, Lien D-H, Brooks GA, Davis RW, Javey A, Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis, Nature 529 (2016) 509–514. doi:10.1038/nature16521. [PubMed: 26819044]

[9]. Anastasova S, Crewther B, Bembnowicz P, Curto V, Ip HM, Rosa B, Yang G-Z, A wearable multisensing patch for continuous sweat monitoring, Biosens. Bioelectron 93 (2017) 139–145. doi:10.1016/j.bios.2016.09.038. [PubMed: 27743863]

[10]. Sempionatto JR, Martin A, García-Carmona L, Barfidokht A, Kurniawan JF, Moreto JR, Tang G, Shin A, Liu X, Escarpa A, Wang J, Skin-Worn Soft Microfluidic Potentiometric Detection System, Electroanalysis 31 (2019) 239–245. doi:10.1002/elan.201800414.

[11]. Martín A, Kim J, Kurniawan JF, Sempionatto JR, Moreto JR, Tang G, Campbell AS, Shin A, Lee MY, Liu X, Wang J, Epidermal Microfluidic Electrochemical Detection System: Enhanced Sweat Sampling and Metabolite Detection, ACS Sensors 2 (2017) 1860–1868. doi:10.1021/acssensors.7b00729. [PubMed: 29152973]

[12]. Kim J, Valdés-Ramírez G, Bandodkar AJ, Jia W, Martinez AG, Ramírez J, Mercier P, Wang J, Non-invasive mouthguard biosensor for continuous salivary monitoring of metabolites, Analyst 139 (2014) 1632–1636. doi:10.1039/C3AN02359A. [PubMed: 24496180]

[13]. Kim J, Jeerapan I, Imani S, Cho TN, Bandodkar A, Cinti S, Mercier PP, Wang J, Noninvasive Alcohol Monitoring Using a Wearable Tattoo-Based Iontophoretic-Biosensing System, ACS Sensors 1 (2016) 1011–1019. doi:10.1021/acssensors.6b00356.

[14]. Bandodkar AJ, Jia W, Yardımcı C, Wang X, Ramirez J, Wang J, Tattoo-Based Noninvasive Glucose Monitoring: A Proof-of-Concept Study, Anal. Chem 87 (2015) 394–398. doi:10.1021/ac504300n. [PubMed: 25496376]

[15]. Kim J, Sempionatto JR, Imani S, Hartel MC, Barfidokht A, Tang G, Campbell AS, Mercier PP, Wang J, Simultaneous Monitoring of Sweat and Interstitial Fluid Using a Single Wearable Biosensor Platform, Adv. Sci (2018). doi:10.1002/advs.201800880.

[16]. Jia W, Bandodkar AJ, Valdés-Ramírez G, Windmiller JR, Yang Z, Ramírez J, Chan G, Wang J, Electrochemical Tattoo Biosensors for Real-Time Noninvasive Lactate Monitoring in Human Perspiration, Anal. Chem 85 (2013) 6553–6560. doi:10.1021/ac401573r. [PubMed: 23815621]

[17]. Mishra RK, Hubble LJ, Martín A, Kumar R, Barfidokht A, Kim J, Musameh MM, Kyratzis IL, Wang J, Wearable Flexible and Stretchable Glove Biosensor for On-Site Detection of Organophosphorus Chemical Threats, ACS Sensors 2 (2017) 553–561. doi:10.1021/acssensors.7b00051. [PubMed: 28723187]

[18]. Bandodkar AJ, O'Mahony AM, Ramírez J, Samek IA, Anderson SM, Windmiller JR, Wang J, Solid-state Forensic Finger sensor for integrated sampling and detection of gunshot residue and explosives: towards 'Lab-on-a-finger', Analyst 138 (2013) 5288–5295. doi:10.1039/c3an01179h. [PubMed: 23865089]

[19]. Kim J, Jeerapan I, Sempionatto JR, Barfidokht A, Mishra RK, Campbell AS, Hubble LJ, Wang J, Wearable Bioelectronics: Enzyme-Based Body-Worn Electronic Devices, Acc. Chem. Res 51 (2018) 2820–2828. doi:10.1021/acs.accounts.8b00451. [PubMed: 30398344]

[20]. Sempionatto JR, Mishra RK, Martín A, Tang G, Nakagawa T, Lu X, Campbell AS, Lyu KM, Wang J, Wearable Ring-Based Sensing Platform for Detecting Chemical Threats, ACS Sensors 2 (2017) 1531–1538. doi:10.1021/acssensors.7b00603. [PubMed: 29019246]

[21]. Mishra RK, Martín A, Nakagawa T, Barfidokht A, Lu X, Sempionatto JR, Lyu KM, Karajic A, Musameh MM, Kyratzis IL, Wang J, Detection of vapor-phase organophosphate threats using wearable conformable integrated epidermal and textile wireless biosensor systems, Biosens. Bioelectron 101 (2018) 227–234. doi:10.1016/j.bios.2017.10.044. [PubMed: 29096360]

[22]. Mahmud MS, Fang H, Carreiro S, Wang H, Boyer EW, Wearables technology for drug abuse detection: A survey of recent advancement, Smart Heal (2018). doi:10.1016/j.smhl.2018.09.002.

[23]. de Jong M, Sleegers N, Kim J, Van Durme F, Samyn N, Wang J, De Wael K, Electrochemical fingerprint of street samples for fast on-site screening of cocaine in seized drug powders, Chem. Sci 7 (2016) 2364–2370. doi:10.1039/C5SC04309C. [PubMed: 29997780]

[24]. French MT, Dunlap LJ, Zarkin GA, McGeary KA, Thomas McLellan A, A structured instrument for estimating the economic cost of drug abuse treatment, J. Subst. Abuse Treat 14 (1997) 445–455. doi:10.1016/S0740-5472(97)00132-3. [PubMed: 9437614]

[25]. Ling W, Mooney L, Hillhouse M, Prescription opioid abuse, pain and addiction: Clinical issues and implications, Drug Alcohol Rev 30 (2011) 300–305. doi:10.1111/j.1465-3362.2010.00271.x. [PubMed: 21545561]

[26]. Suzuki J, El-Haddad S, A review: Fentanyl and non-pharmaceutical fentanyls, Drug Alcohol Depend 171 (2017) 107–116. doi:10.1016/j.drugalcdep.2016.11.033. [PubMed: 28068563]

[27]. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G, E. Release, Drug and Opioid-Involved Overdose Deaths — United States, 2013 – 2017, Morb. Mortal. Wkly. Rep 67 (2019) 1419–1427. doi:10.15585/mmwr.mm675152e1.

[28]. Maurer HH, Advances in analytical toxicology: the current role of liquid chromatography?mass spectrometry in drug quantification in blood and oral fluid, Anal. Bioanal. Chem 381 (2005) 110–118. doi:10.1007/s00216-004-2774-z. [PubMed: 15309372]

[29]. Harper L, Powell J, Pijl EM, An overview of forensic drug testing methods and their suitability for harm reduction point-of-care services, Harm Reduct. J 14 (2017) 52. doi:10.1186/s12954-017-0179-5. [PubMed: 28760153]

[30]. Haddad A, Comanescu MA, Green O, Kubic TA, Lombardi JR, Detection and Quantitation of Trace Fentanyl in Heroin by Surface-Enhanced Raman Spectroscopy, Anal. Chem 90 (2018) 12678–12685. doi:10.1021/acs.analchem.8b02909. [PubMed: 30247896]

[31]. Ahmar H, Fakhari AR, Tabani H, Shahsavani A, Optimization of electromembrane extraction combined with differential pulse voltammetry using modified screen-printed electrode for the determination of sufentanil, Electrochim. Acta 96 (2013) 117–123. doi:10.1016/j.electacta.2013.02.049.

[32]. Wang G, Huynh K, Barhate R, Rodrigues W, Moore C, Coulter C, Vincent M, Soares J, Development of a homogeneous immunoassay for the detection of fentanyl in urine, Forensic Sci. Int 206 (2011) 127–131. doi:10.1016/j.forsciint.2010.07.022. [PubMed: 20801588]

[33]. Hubble LJ, Wang J, Sensing at Your Fingertips: Glove-based Wearable Chemical Sensors, Electroanalysis (2018) elan.201800743. doi:10.1002/elan.201800743.

[34]. Drug Enforcement Administration, DEA Issues Nationwide Alert On Fentanyl As Threat To Health And Public Safety, (2015). https://www.dea.gov/press-releases/2015/03/18/dea-issues-nationwide-alert-fentanyl-threat-health-and-public-safety.

[35]. Opallo M, Lesniewski A, A review on electrodes modified with ionic liquids, J. Electroanal. Chem 656 (2011) 2–16. doi:10.1016/j.jelechem.2011.01.008.

[36]. Scholz F, Lange B, Abrasive stripping voltammetry — an electrochemical solid state spectroscopy of wide applicability, TrAC Tren. Anal. Chem 11 (1992) 359–367.

[37]. Goodchild S, Hubble L, Mishra R, Li Z, Yugender K Barfidokht A, Shah R, Bagot K, McIntoshe A, Wang J, Ionic liquid-modified disposable electrochemical sensor strip for analysis of fentanyl, Anal. Chem, 91 (2019) 3747–3753. doi: 10.1021/acs.analchem.9b00176. [PubMed: 30773004]

Research Highlights

- Field screening of opioids with a wearable glove-based electrochemical sensor

- Rapid "swipe, scan, and detect" operating procedure

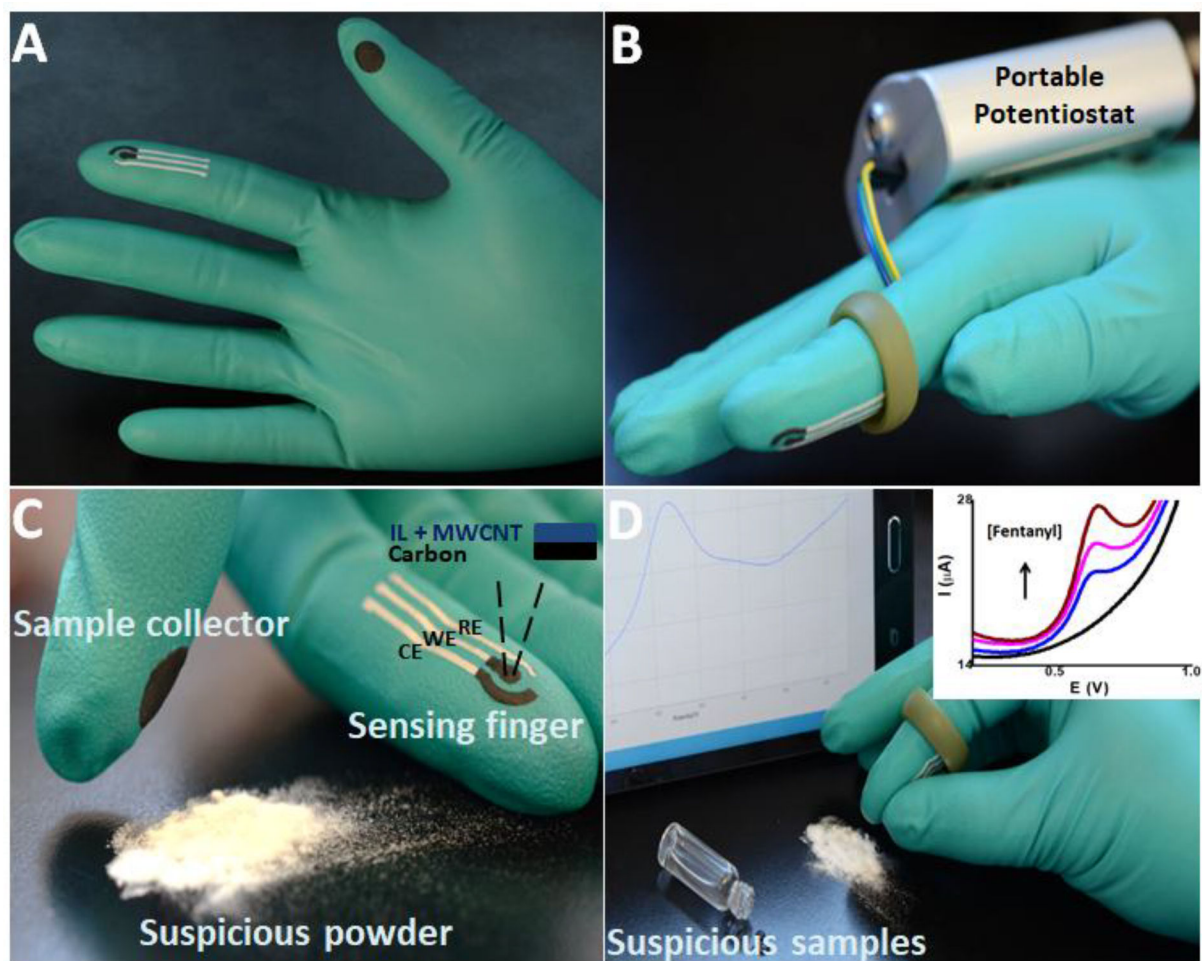- Progress towards a complete forensic "Lab-on-Glove"

Figure 1.
Overview of the proposed Lab-on-a-Glove concept (swipe, scan, and sense) for on-site detection of fentanyl; (A) Photograph of glove containing sensing finger modified with ionic liquid/MWCNT composition and sample collector. (B) Image showing the glove-based sensor with a portable electroanalyzer (back-view). The electrodes are connected via wires and a modified ring to PalmSens for on-site detection with wireless communication to a smartphone for rapid analysis and reporting of the SWV results. (C) Image showing suspicious sample collection in powder phase. (D) Joining of thumb (collector) and sensing (index) fingers after swiping a powder sample; inset shows the voltammograms of direct fentanyl detection in dry/liquid samples.
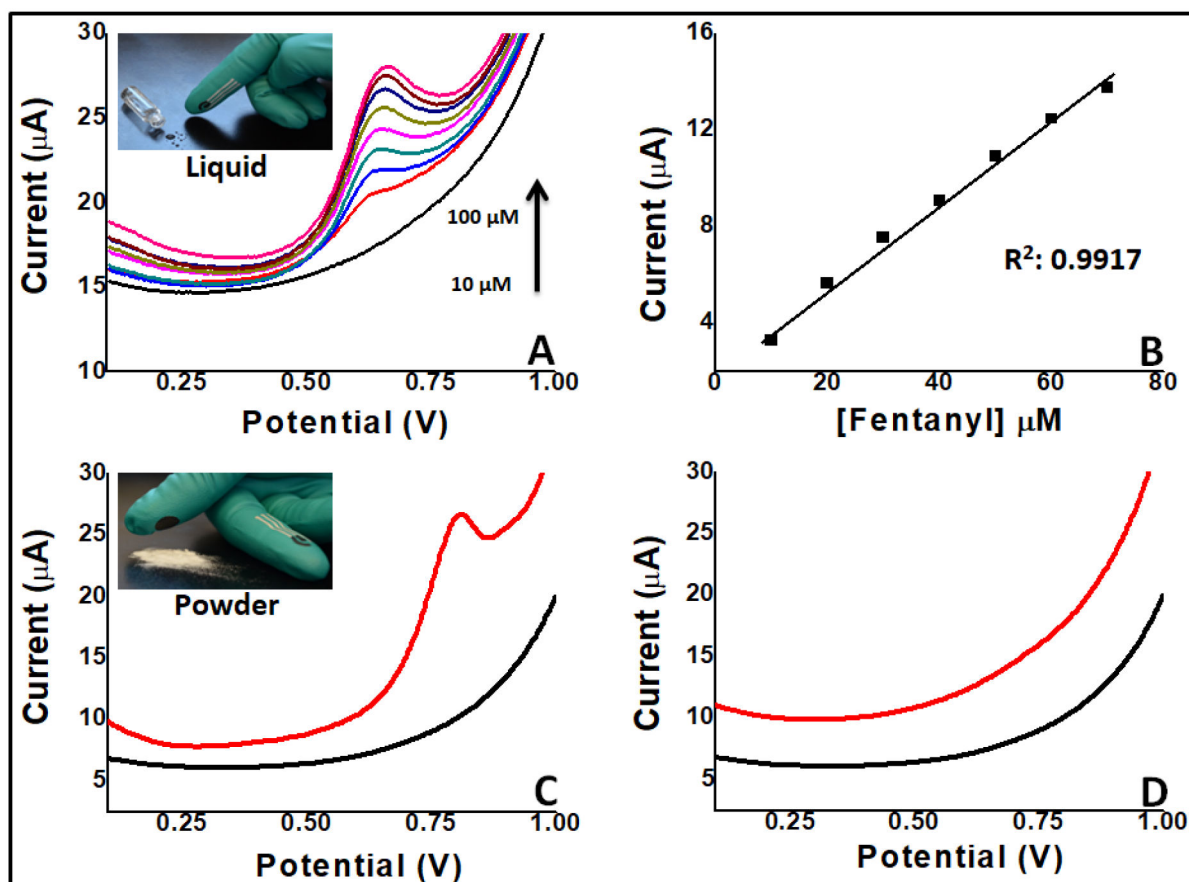
Figure 2:
Electrochemical characterization of the glove-based sensor for fentanyl samples in liquid and powder forms. (A) Square wave voltammetric response of the glove sensor to increasing fentanyl concentrations from 10 to 100 μM (10 μM interval) in PBS (0.1 M, pH 7.4). (B) Corresponding calibration plot. (C) Sensor response toward screening powder fentanyl samples, as the residue of 5 μL fentanyl stock solution (the black curve is the signal prior to fentanyl sample swiping). (D) Control experiments swiping the surface in the absence of fentanyl.
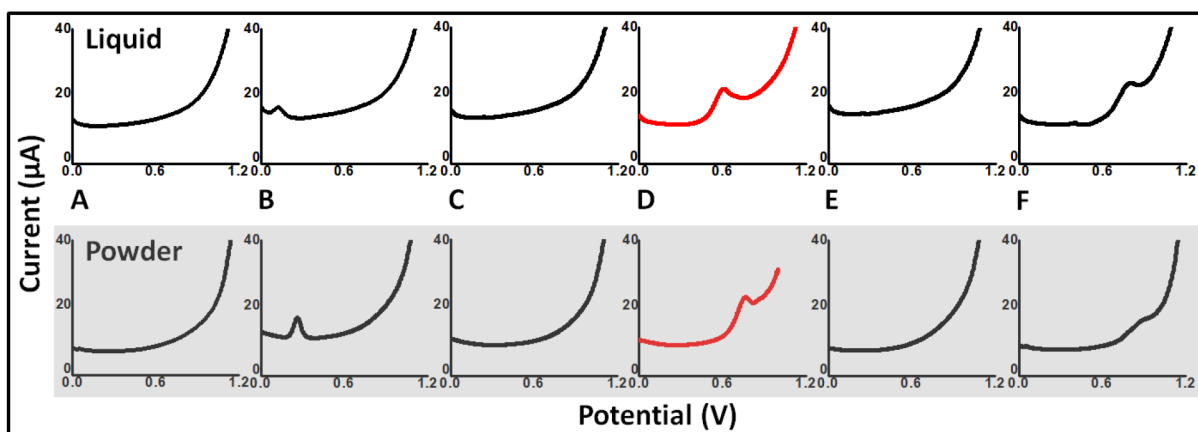
Figure 3:
Performance of the glove-based sensor toward potential interferences and cutting agents. Square wave voltammograms of (A) phosphate buffer solution and 100 μM of (B) acetaminophen, (C) caffeine, (D), fentanyl, (E) glucose and (F) theophylline in both liquid (top) and powder (bottom) forms.
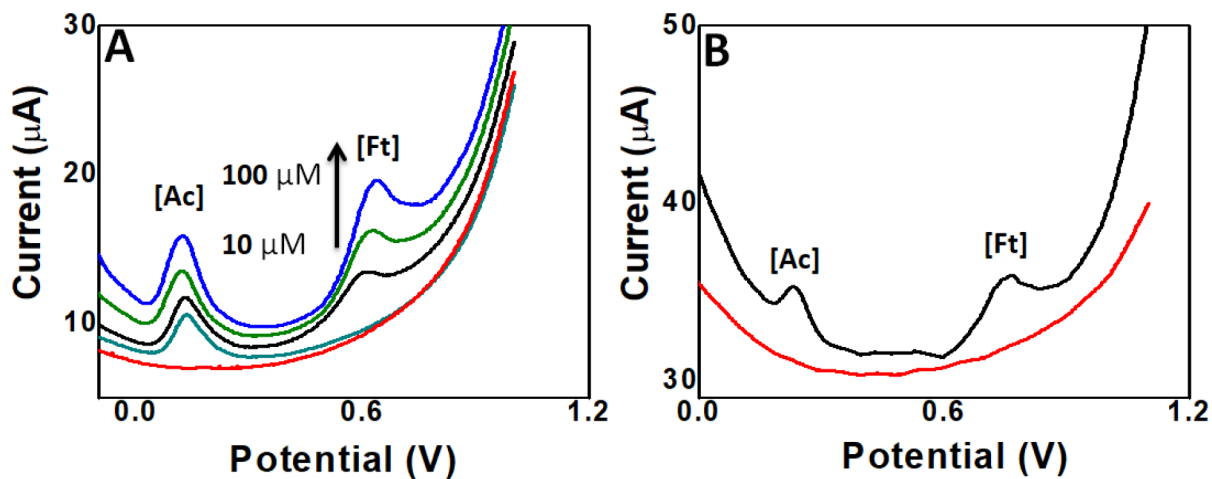
Figure 4:
Fentanyl response in a mixture of cutting agents. (A) Square wave voltammetric responses of liquid fentanyl (Ft) (10 to 100 μM) in a mixture containing 100 μM (fixed concentration) cutting agents of acetaminophen (Ac), caffeine, and glucose in PBS (0.1 M, pH 7.4). (B). Fentanyl response in a mixed powder (100 μM of fentanyl, acetaminophen, caffeine, and glucose were dried and formed the powder).