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Wearable Electrochemical Alcohol Biosensors

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Abstract

The rapid development of wearable sensing platforms in recent years has led to an array of viable monitoring applications for various target analytes. As a significant biomarker with high impact in diverse areas, the reliable on-body detection and continuous monitoring of alcohol has become a focus of many such systems. Currently, several commercial sensing platforms are available that are capable of transdermal monitoring of alcohol consumption using insensible sweat. Drawbacks of existing alcohol sensing platforms that apply this sensing strategy have led to efforts in developing wearable biosensors capable of real-time alcohol detection in sampled biofluids such as sensible sweat and skin interstitial fluid. This review discusses the current trends in wearable electrochemical alcohol biosensing and highlights recent advances in such systems toward continuous, real-time monitoring of alcohol consumption. Our perspective on this important field is given with an outlook on the future of wearable electrochemical alcohol biosensors.

Keywords

Wearable biosensors; electrochemical detection; alcohol monitoring; enzyme-based biosensors; epidermal sensing; blood alcohol concentration

Introduction

Alcohol consumption is common and widespread throughout society with millions of people consuming regularly [1]. Such use has promoted a wide array of adverse impacts on personal health and economic factors [2–4]. Thus, monitoring of alcohol abuse and effective, real-time alcohol detection represent substantial concerns for personal and automobile safety as well as in clinical settings since alcohol use is reported as a contributing factor in a bevy of health complications including fetal alcohol spectrum disorders, various types of cancer, cardiovascular disease, stroke, liver cirrhosis, multiple psychiatric comorbidities, and pancreatitis among others [3]. Currently, the most consistent measure of alcohol intoxication is direct evaluation of blood alcohol concentration (BAC) [5–10]. This detection method relies on invasive blood sampling, which is not appropriate for continuous monitoring applications. Thus, the reliable and convenient determination of BAC through non-invasive

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or minimally-invasive means (*i.e.* not requiring the sampling of blood) is of significant interest for clinical, safety, and forensic applications as well as for safe recreational consumption and basic research [11].

The most common approach for real-time determination of alcohol intoxication currently applied is the use of breath-analyzers to indirectly estimate BAC through measurement of breath alcohol concentration (BrAC) by applying Henry's law. Although this method can be applied in the field via portable breath-analyzers, the resulting measurements suffer from inaccuracies due to substantial interferences from external and internal factors such as humidity, temperature, subject physiological variation, contamination from compounds present in the mouth (*i.e.* residual alcohol vapor), and environmental vapors as well as by inconsistent system calibration [12–14]. Further, the sample collection and sensing principles of the breath-analyzer require purposeful action by the user, which limits continuous monitoring applicability. Alternative strategies are thus necessary to provide a convenient, continuous, accurate and robust method of alcohol intake sensing/monitoring in different settings. This capability could promote not only responsible personal alcohol use, but also allow reliable reporting for healthcare and clinical applications. Such necessity has led to efforts on developing alcohol biosensors on wearable platforms using non-invasive/minimally-invasive biofluids for continuous monitoring of BAC.

Wearable sensing platforms have garnered significant recent research attention along with an increased commercial presence [15–19]. The utilization of electrochemical biosensors in these systems has been a major topic of such research, starting with the introduction of an epidermal sweat lactate amperometric biosensor based on immobilized lactate oxidase [20]. Since this report, wearable sensing devices have been designed to detect target analytes in sampled biofluids including sweat, interstitial fluid (ISF), tears and saliva, which have the potential to provide a direct measure of concurrent analyte levels in blood depending on a valid correlation between concentrations in the two fluids [16]. Thus, the monitoring of alcohol concentrations in biofluids, such as urine, saliva, sweat and ISF, could be achieved without necessitating invasive blood sampling toward real-time measure of alcohol intoxication [8,21,22]. Significant efforts have hence been put forth to develop alcohol sensors targeting detection in these biofluids [11]. The rapid pace of wearable sensors development has led to a new generation of epidermal electrochemical biosensors that impart a 'wear-and-forget' functionality, without compromising wearer comfort or causing distraction from routine activities [17]. Several wearable sensing platforms have been designed recently for the detection of alcohol, focusing primarily on monitoring the sweat and ISF fluids.

Electrochemical detection strategies have been applied for detection of alcohol in sweat and ISF due to the advantageous sampling possibilities of these biofluids, as discussed herein. Alcohol can be electrochemically measured in biofluids by leveraging direct ethanol oxidation at non-enzymatic catalytic electrodes (*e.g.* platinum, gold, etc.) or by utilizing recognition by bioreceptors (*i.e.* enzyme, antibody, etc.) immobilized onto the electrode surface in the case of alcohol biosensors [23]. Biosensors use these bioreceptors to recognize alcohol or an alcohol metabolite via specific reactions coupled with transduction of this biorecognition event to a detectable signal. Enzymatic alcohol biosensors have been widely

used for the measurement of alcohol since the pioneering studies of Guilbault [24] and Christian [25] in the 1970s using the enzymes alcohol oxidase (AOX) or alcohol dehydrogenase (ADH). AOX catalyzes the oxidation of ethanol according to the reaction in Equation 1 to generate hydrogen peroxide (H₂O₂), which can be electrochemically detected at the electrode transducer (Figure 1ii):

Alternatively, ADH catalyzes the reversible oxidation of ethanol to acetaldehyde along with the external coenzyme nicotinamide adenine dinucleotide (NAD) according to Equation 2:

In this case, the formed NADH can be amperometrically (anodically) monitored to detect ethanol level, while regenerating the NAD⁺ cofactor.

For wearable applications, however, AO_X is most commonly applied as it does not require the presence of external cofactor such as NAD⁺ used with ADH and hence is not subject to related stability and selectivity issues [26,27]. The anodic detection of the NADH product of the ADH reaction requires large overvoltage and encounters surface fouling associated with the accumulation of reaction products [28,29]. Such NADH-based ethanol detection may thus require a redox mediator that may also hinder wearable applications. Alternately, alcohol can also be monitored indirectly by measuring a metabolite of alcohol, which includes ethyl sulfate (EtS), ethyl glucuronide (EtG) and acetaldehyde. Acetaldehyde can be electrochemically measured using aldehyde dehydrogenase (AldDH) [30]. Since other minor metabolites, EtS and EtG, are non-oxidative products, these are mostly coupled with LC/MS. Recently, EtG has been integrated with immunoassay-based detection systems for electrochemical detection [31]. Electrochemical alcohol detection systems have been integrated with various types of wearable platforms for non-invasive and minimally-invasive alcohol sensing applications. These sensing principles and distinctions are exhibited in Figure 1.

This review discusses recent studies and new device targeting on-body electrochemical alcohol monitoring with emphasis on major advances toward epidermal biosensing in sweat and ISF. Recent developments of such wearable alcohol sensing systems are discussed to give a descriptive overview of the current status of this exciting and important field along with the current state-of-the-art in wearable electrochemical alcohol sensing. Finally, our perspective on the remaining challenges and future directions of wearable electrochemical alcohol biosensors is presented.

Sweat-based alcohol detection

The epidermis is a highly advantageous site for biofluid sampling in wearable sensing systems as it covers a vast majority of our bodies. In particular, epidermal sweat sampling

has been extensively examined for wearable sensing applications due to the density of sweat glands across the body and the array of significant biomarkers sweat contains (*i.e.* alcohol, glucose, lactate etc.) [32,33]. Although, epidermal devices designed to sense target analytes in liquid sweat require the excretion of sweat to the outer skin surface, various methodologies have been shown to achieve sweat generation in a wearable device in real-time [34–36]. Importantly, sweat alcohol concentrations have been shown to exhibit a close correlation with concurrent blood alcohol levels, which has promoted development of the wearable sweat alcohol sensing platforms discussed herein [21].

The Pingarrón group demonstrated a wearable alcohol monitoring device that proved capable of electrochemically detecting alcohol in chemically induced sweat via bi-enzymatic reaction (Figure 2A) [37]. This system utilized the commercially available Macroduct 3700-SYS sweat sampling unit from Wesnor Inc. to induce sweat generation through iontophoretic delivery of the sweat stimulant pilocarpine [38]. The process of iontophoresis involves applying a mild electric current between two skin-mounted electrodes that causes the delivery of positively charged compounds (*i.e.* pilocarpine) across the skin to stimulate sweat production without exercise or thermal heating [39]. Such pilocarpine induced sweat production is widely utilized for practical sweat sampling in an individual at rest or during their daily routine, compared to exercise or thermal heating. After the pilocarpine delivery, ethanol in generated sweat is electrochemically measured. The H₂O₂ generated by AOx (Equation 1) was thus reduced by horseradish peroxidase (HRP) to form water and an oxidized form of HRP, which was subsequently reduced by electrochemically regenerated ferrocene mediator to yield a detectable signal (schematic depiction of reaction mechanism shown in Figure 2Ai). This ferrocene-mediated, dual enzyme electrochemical detection approach facilitated low potential amperometric detection of alcohol at 0.00 V (vs Ag/AgCl). The measured changes in sweat alcohol concentrations correlated to concurrent blood levels, as validated using gas chromatography. The performance of this system was further demonstrated with 40 human subjects to show this correlation in a clinical setting (Figure 2Aii). This work demonstrated a wearable alcohol sensing system for either a continuous or single measurement approach, but further integration with iontophoretic sweat generating system and user-friendly electronics can be improved. These results further corroborated the rapid equilibrium of ethanol across the sweat gland epithelium in relation to BAC with no time-lag, as proposed in previous studies [21].

Wang et al. demonstrated a non-invasive tattoo-based alcohol detection system integrating pilocarpine-based iontophoretic sweat generation and amperometric biosensing on a single platform (Figure 2B) [40]. The printed electrode layout on temporary tattoo paper obviated the need for separate sweat-generation and sensing devices through utilization of screen printed fabrication. Iontophoresis was carried out using printed Ag/AgCl electrodes while selective alcohol recognition in the generated sweat was achieved with printed Prussian-Blue containing carbon electrodes modified with AOx. The flexible tattoo-based system could withstand severe mechanical strains expected from bodily activity, ensuring reliable performance in the face of the rigors of daily human wear. In this system, Prussian-Blue mediated the electrochemical reduction of H₂O₂, the product of the AOx-catalyzed enzymatic reaction between in the sampled sweat, to provide selective alcohol detection with operation at low voltages (−0.2 V vs Ag/AgCl) (Figure 2Bi). Hence, electroactive sweat

constituents had negligible effect upon the response, compared to common platinum-based detection. The tattoo-based platform was integrated with a flexible printed circuit board that provided wireless electrochemical analysis of alcohol via Bluetooth transmission of processed data to a lap-top (Figure 2Bii). The device was further proven capable of detecting alcohol intake in human subjects with verification of concurrent changes in BAC (Figure 2Biii).

Both discussed non-invasive sensing systems demonstrated the rapid progress being made in wearable electrochemical biosensors with alcohol detection in excreted sweat, obviating the extended time-lag between alcohol intake and detection inherent to insensible-sweat-based transdermal alcohol sensors. However, challenges yet remain toward continuous monitoring applications as detection in generated sweat can only be achieved as long as sweat is produced, which is generally limited to 30-120 min using pilocarpine [34,37]. Further, the efficiency of iontophoresis and resulting sweating rate can vary, and can affect direct correlations between measured alcohol concentrations with concurrent BAC.

An alternative alcohol detection strategy in sweat was employed by Prasad et al., who reported on a wearable electrochemical immunosensor targeted at detection of EtG, an alcohol (ethanol) metabolite used for monitoring of alcohol consumption lifestyle (Figure 3A) [31]. EtG is a minor metabolic product of alcohol formed in the liver and can be detected for up to one day after moderate alcohol consumption or for up to two to four days after heavy consumption, which makes this analyte of considerable interest in abstinence monitoring situations. The developed system was composed of two co-planar electrodes made up of gold or zinc oxide with monoclonal EtG antibodies immobilized via thiol chemistry (Figure 3Ai). These electrodes were patterned onto rigid and flexible substrates and combined with a portable LED display toward wearable applications (Figure 3Aii). EtG was detected using a chemi-resistive sensing mechanism in which the impedance measured between the two electrodes, with an applied AC voltage would increase in response to higher levels of EtG owing to the EtG binding to the immobilized specific antibody. Such antibody-based sensing platforms provide remarkable specificity due to the binding nature of antibodies, but regeneration of the unbound antibody is necessary for reuse. This device was shown capable of detecting EtG over a physiologically relevant range in various samples of pooled human sweat using both the rigid and flexible electrode substrates (Figure 3Aiii). Such a bioaffinity sensing system represents a viable alternative to direct alcohol detection for specific applications, but will require integration with an effective sweat sampling method for reliable on-body use as well as thorough validation with measured BAC levels.

ISF-based alcohol detection

The reported non-invasive alcohol detection platforms exhibited promising performance, but required the additional step of biofluid generation in order for sampling and subsequent analysis to occur. An alternative approach is to measure alcohol concentrations continuously through constant interaction with the biofluid of interest. The concentrations of metabolites in ISF can be correlated to concurrent levels in blood due to the nature of their diffusion from the bloodstream [41]. ISF surrounds the viable cells within skin tissue to provide necessary nutrients supplied through blood. Due to this mechanism, ISF alcohol levels

display a close correlation with concurrent concentrations in blood [22]. Wang et al. developed a microneedle-based minimally-invasive sensing platform for analyzing alcohol concentrations in ISF (Figure 3B) [42]. Microneedles readily access the ISF to facilitate transdermal monitoring. This amperometric microneedle biosensor detected alcohol in artificial ISF using AOX immobilized at the tip of the microneedle, which contained a platinum wire electrode transducer (Figure 3Bi). In this system, H₂O₂ generated by the reaction of AO_X with alcohol (Equation 1) was oxidized at the platinum working electrode using an applied voltage of +0.6 V (vs Ag/AgCl). Polymeric membrane coatings of poly(o-phenylenediamine), chitosan and Nafion was used to minimize interferences from applied potential electroactive compounds, present in the sampled biofluid (*i.e.* ascorbic acid, uric acid etc.). The microneedle design allows constant access to the constituents of ISF for continuous monitoring. Toward this goal, the microneedle sensing array was shown capable of detecting varying alcohol concentrations in artificial ISF after penetration through mice skin (Figure 3Bii). However, successful operation in human subjects is required for validated performance as well as extensive large-scale verification of alcohol monitoring with concurrent BAC measurements. A summary of the wearable electrochemical alcohol biosensors discussed here is given in Table 1.

Transdermal alcohol monitoring platforms

While the majority of alcohol consumed is metabolized by the liver, approximately 1% is excreted through the skin as vapor state insensible sweat [6,43]. The concentration of alcohol permeating through the epidermis in this manner can be detected by wearable devices, termed transdermal sensors, and has exhibited validated correlations against BrAC and BAC (Figure 1A) [44–46]. Several sensing platforms utilizing this method of alcohol monitoring have been developed with most clinical reports focusing on two devices: the Secure Continuous Remote Alcohol Monitor from Alcohol Monitoring Systems, Inc. (SCRAMTM; Figure 4A); and the Wrist Transdermal Alcohol Sensor from Giner Inc. (WrisTASTM; Figure 4B) [46–48]. The SCRAMTM is designed as an ankle bracelet with a sensor compartment and a digital signal processing compartment, which transmits the collected data to an in-home modem. This platform has been implemented by law enforcement personnel to monitor individuals with alcohol-related offenses, and as such, contains tamper detection safeguards including temperature and skin contact sensors as well as a locked strap. The SCRAMTM detects alcohol in insensible sweat using an air pump to collect vapor at the skin surface that is analyzed with a platinum-based electrochemical fuel-cell detector to determine alcohol content through catalytic alcohol oxidation (Figure 1Bi). The WrisTASTM is designed as a wrist bracelet that also contains skin contact and temperature sensors, but is removable as it was primarily designed for use in medical settings. This device samples alcohol at the surface of the skin, and detects it via hydrated platinum electrochemical sensor to measure alcohol content also through platinum-catalyzed oxidation, with measurements manually downloaded to a computer. Both devices have been the subject of multiple clinical trials to evaluate efficacy of use [49–53].

As wearable electronics have grown in popularity more recently, coupled with a drive by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), a part of the National Institute of Health (NIH), increased attention has been given to wearable transdermal

alcohol monitoring platforms with several smaller and sleeker wrist-worn devices being developed. The BACtrack Skyn wearable alcohol monitor from BACtrack (Figure 4C), which utilizes a fuel-cell type alcohol sensor, can be coupled with a smartphone App to track estimated BAC and integrated into a standalone wearable or into the band of a smartwatch. The Proof™ alcohol tracking wearable from Milo Sensors (Figure 4D) utilizes an enzymatic electrochemical biosensor cartridge for alcohol detection, which can be coupled to a smartphone App that targets safe recreational alcohol consumption with an integrated social aspect. The amperometric detection mechanism used applies dual enzymatic reactions of AOX and HRP coupled with ferrocene mediation [54]. Additionally, the Quantac Tally wrist-worn alcohol monitor from Quantac (Figure 4E) combines alcohol monitoring data in its coupled smartphone App with health-related metrics to inform the wearer of personalized insights into health impacts of their alcohol consumption.

Transdermal alcohol sensors have proven useful in multiple scenarios with new more advanced platforms rapidly being developed. However, these devices suffer from an inherent delay between changes in BAC being reflected by the monitor of one or more hours due to the time required for alcohol to be expelled as insensible sweat [55,56]. Additionally, transdermal vapor-based alcohol sensors may yield false signals, rising from external alcohol-containing vapors (*i.e.* bar scenario, paint, etc.) as well as from alternate components found in insensible sweat due to the non-specific nature of the electrochemical detection method (*i.e.* non-specific oxidation at the sensing electrode, particularly non-enzymatic platinum-based sensors) [45,46,53]. In many instances, real-time monitoring of a wearer's BAC is preferred, hence promoting extensive research efforts into wearable electrochemical alcohol sensors that directly monitor alcohol concentrations in biofluids such as (sensible) sweat and ISF [47].

Conclusions

The development of wearable electrochemical alcohol biosensors has accelerated in recent years as a result of trends in commercial and researched technologies. The wearable platforms discussed herein highlight the recent advances in this area and represent the current state-of-the-art in wearable electrochemical alcohol biosensors. These devices have been designed to meet the needs of a variety of applications ranging from law enforcement and addiction studies to alcohol lifestyle monitoring, health and safety. In order to provide user-friendly platforms capable of continuous detection, recent efforts have focused on measuring alcohol in sweat and ISF using non-invasive or minimally-invasive detection methodologies. Such wearable monitoring platforms could provide extremely useful information for a wide variety of beneficial applications with significant potential impact due to the prevalence of alcohol-related costs and health issues. Preliminary evaluations of these wearable platforms have been proven useful with demonstrated correlation to BAC and on-body sampling of alcohol in sweat and ISF that could reduce potential interferences observed in currently employed breath-analyzers (*i.e.* environmental alcohol vapors, residual alcohol concentrations, etc.).

Continued progress toward increased practical application opportunities to advance these wearable devices beyond proof-of-concept reports will require overcoming remaining

challenges in wearable biosensing. Successful application of these technologies relies on the accuracy and reliability of measurements, which are commonly impacted by the fragility of the bioreceptor (enzyme/antibody), uncontrolled operational conditions (*i.e.* temperature, humidity, etc.), surface fouling and contamination from environmental factors or the carry-over from previously sampled fluids. Work toward addressing these issues will focus on ensuring reliable detection of alcohol concentrations through multiplexed sensing, enhanced biofluid sampling methodologies such as microfluidic technologies, and optimized enzyme/antibody immobilization methods for consistent long-term operational and storage stability [34,35]. Such efforts should also center on addressing the need for extensive on-body calibrations to report accurate readings of BAC in a real-time manner. Further, the discussed sweat-and ISF-based wearable electrochemical platforms require seamless integration with smartphone apps for continuous tracking and display of the BAC, along with the appropriate data security and privacy. Such devices can be coupled with transportation services (*i.e.* interlock devices) or health tracking information for decreased instances of DUI or other dangerous side effects of alcohol consumption. Wearable alcohol detection approaches should also be expanded to include other readily sampled biofluids, such as tears and saliva, as well as focus on improvement of detection reliability, reduction of the sensing time lag, and improved stability for extended monitoring periods. The future of wearable alcohol sensing devices shows promising capabilities relying on successful performance validation in large-scale on-body trials relative to concurrent changes in BAC as well as the integration of such devices into textile-based platforms or fashion accessories for effective incorporation into a wearer's daily life. These advances will be realized through a multidisciplinary effort between the scientific and engineering communities in collaboration with clinical research.

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Highlights

- Review of recent advances in wearable electrochemical alcohol sensors
- Electrochemical alcohol detection strategies in biofluids
- Toward continuous monitoring of alcohol intake
- Wearable sampling of alcohol in sweat and interstitial fluid
- Real-time sensing of alcohol intoxication for health, clinical or research purposes

A. Alcohol in non-invasive bio-fluids

B. Electrochemical sensing alcohol

i) Fuel-cell type

ii) Enzyme-based type

iii) Immunoassay type

Figure 1: Summary of main concepts discussed.

A) Schematic depiction of sweat and ISF physiology in the body and sampling methodologies for sensing. B) Alcohol detection paradigms for i) fuel-cell type alcohol sensors, ii) enzyme-based alcohol biosensors, and iii) immunoassay type alcohol immunosensors.

Figure 2: Wearable non-invasive sweat alcohol sensors.

A) i) Schematic representation of bi-enzymatic electrochemical alcohol detection cell for monitoring sweat alcohol concentration after iontophoretic stimulation with depiction of alcohol recognition reactions. ii) Comparison of measured sweat alcohol levels in 40 human subjects with concurrent BAC. Reproduced with permission from Ref. [**37]. Copyright (2014) Elsevier. **B)** i) Schematic representation of screen-printed, wearable iontophoretic delivery and alcohol detection platform with depictions of pilocarpine delivery, on-body application, and alcohol recognition reactions. ii) Depiction of wireless transmission of alcohol sensing data using flexible printed circuit board. iii) Collected on-body alcohol detection data with human subjects, with or without drinking, correlated to concurrent BAC. Reproduced with permission from Ref. [**40]. Copyright (2016) American Chemical Society.

Figure 3: Alcohol lifestyle and ISF alcohol monitoring.

A) i) Schematic representation of EtG immunosensor design with EtG antibody immobilization. ii) Depiction of immunosensor patterning onto flexible or rigid substrate and integration with portable LED display. iii) Evaluation of EtG immunosensor on flexible or rigid substrate in pooled human sweat at varying EtG concentrations. Reproduced with permission Ref. [**31]. Copyright (2016) Macmillan Publishers Limited. **B)** i) Schematic representation of microneedle-based alcohol sensing array with layered functionalization of working electrode. ii) Evaluation of microneedle-based alcohol sensing array in artificial ISF operating through mice skin. Reproduced with permission Ref. [**42]. Copyright (2017) Elsevier.

Figure 4: Transdermal alcohol monitoring platforms.

Alcohol monitoring devices utilizing insensible sweat. **A)** Secure Remote Alcohol Monitor (SCRAM™) from Alcohol Monitoring Systems, Inc. Reproduced with permission from Alcohol Monitoring Systems, Inc. Copyright (2018) (left). Reproduced with permission from Ref. [47]. Copyright (2012) Research Society on Alcoholism (right). **B)** Wrist Transdermal Alcohol Sensor (WrisTAS™) from Giner, Inc. Reproduced with permission from Ref. [47]. Copyright (2012) Research Society on Alcoholism **C)** BACtrack Skyn from BACtrack. Reproduced with permission from BACtrack. Copyright (2018). **D)** Proof™ alcohol tracking wearable by Milo Sensors. Reproduced with permission from Milo Sensors Inc. Copyright (2018).

Table 1

Summary of wearable electrochemical alcohol biosensors.

Platform	Biofluid	Electrochemical method	Sensitivity ($\mu\text{A}/\text{mM}$)	Linear range (mM)	On-body [Y/N]	Ref.
Transdermal graphite-Teflon-AOx-HRP-ferrocene composite electrode placed after iontophoretic sweat stimulation	Sweat	Chronoamperometry at 0.0 V vs Ag/AgCl	0.07 ± 0.003	0.01 - 13.0	Y	[37]
Screen printed AOx-Prussian Blue epidermal tattoo with integrated iontophoretic sweat stimulation	Sweat	Chronoamperometry at -0.2 V vs Ag/AgCl	0.36 ± 0.009	3.0 - 36.0	Y	[40]
Flexible co-planar gold or zinc oxide electrodes for bioaffinity-based epidermal EtG immunosensing	Sweat	Chemi-resistive impedance	-	0.001 - 100 $\mu\text{g}/\text{L}$ EtG	N	[31]
Microneedle-based AOx-platinum electrode	ISF	Chronoamperometry at 0.8 V vs Ag/AgCl	0.045 nA/mM	5.0 - 80.0	N	[42]