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Electrochemical Wearable Sensors for Wound Monitoring

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ABSTRACT

Wound healing in any kind of wound, specifically chronic ones could be affected by Infection which represents the key complication. There are presently certain restrictions to the procedures that are utilized for establishing a wound-infection clinical diagnosis. Therefore, novel, rapid, and user-friendly approaches for wound infection diagnosis require to be extended. To this purpose, electrochemical wearable sensors for infection diagnosis have been expanded recently. These sensors have been incorporated into the wound dressings that have been utilized to therapy and protect the wound and are capable to indicate certain biomarkers that could be associated with the wound infection existence. Among these biomarkers, the most frequently utilized ones are pH and uric acid, however, a plethora of others (lactic acid, oxygenation, inflammatory mediators, bacteria metabolites, or bacteria) have also been determined by electrochemical wearable sensors.

Keywords: Electrochemical Sensors; Wound Infection Biomarkers; Wound Status; Nanostructured Materials-Enabled Sensors

Introduction

Infection demonstrates the main complication of both acute and chronic wounds, with an adverse effect on wound healing, living patient quality, and economic resources [1,2]. However, the wound infection general effect is tough to assess, it has been evaluated that surgical site infections in the UK alone affect 3–4% of surgery patients, cost an average €5800 for each patient, and reason an average death rate of 5% [3]. A retrospective investigation from 2018 in the USA showed that around 8.2 million people suffered from with or without infection wounds. The highest expenses of therapy were related to surgical wounds and chronic foot ulcers. Chronic wounds demonstrate a growingly problematic area of wound management, due to issues like an elderly population and the increasing prevalence of Diabetes and obesity [2]. In this framework, it is essential to diagnose wound infection immediately in order to ensure the greatest therapy course for the patient. Presently used diagnostic approaches have been described via clinical inspection and microbiological assays [4-6]. In spite of being regularly utilized, these procedures include several defects like inaccuracy, require for traumatic bandage removal, and dependence on the physician's expertise in the case of clinical examination. Some restrictions of microbiological evaluation are long analysis periods, invasive methods in the case of microbiological assays accomplished on biopsy tissue, and lack of recognition of bacteria invading deep tissues in the case of swab cultures [4]. A substitute infection diagnosis technique is the recognition of certain biomarkers in the wound environment.

In order to increment patient comfort and eliminate the possibly traumatic bandage removal procedure for clinical inspection, a perfect solution for biomarker monitoring is the incorporation of wearable sensors for infection biomarkers in wound bandages. Various proof of principle examples of such sensors has been lately issued, however, up to the present time, due to Specific restrictions none of these methods has been clinically accomplished on a large scale. The expansion of wearable devices has been faced with a mixed variety of challenges concerning the materials utilized, power sources, and information transition [5]. The combined substances require to be biocompatible and tailored thus that they could adapt to the skin's curvilinear surface [5,6]. Furthermore, they require to be flexible and resistant in order to certify the user's free movement [7]. Power sources like batteries are tough to miniaturize and integrate into wearable devices [6], though are necessary for their operation and appropriate functioning, therefore it is essential to find a way to tackle this problem. Several challenges have been also proposed via proper design and secure ways of wireless transmission between the sensor and devices like laptops and smartphones [5,7]. These kinds of technologies have been presently exhibited by Bluetooth [5,8], Near-Field-Communication (NFC) [9-11], and radiofrequency identification (RFID) [9-11]. In spite of all these obstacles, the expansion of the sensor for point-of-care (POC) usage is a promising path for analytical procedures field. The emersion of wearable commercial devices for biological parameters (heart rate, blood pressure, movement) demonstrates the substantial role wearable devices will play in precision medicine.

Electrochemical Sensors

According to The International Union of Pure and Applied Chemistry (IUPAC), chemical sensors are defined as devices that provide the chemical information transformation like the concentration of a specific sample component, into an analytically useful signal which could be apperceived or recorded and utilized to determine the attendance of the analyte in unidentified samples [12]. Two separated but codependent functional parts have been included in a typical chemical sensor: a receptor part and a transducer part [12]. The receptor comprises either biomimetic elements like aptamers, nanozymes, or molecularly imprinted polymers (MIPs) [13], or biocomponents like enzymes, and antibodies in this case we have a biosensor [14]. Apart from its nature, the receptor's role is to convert the analyte concentration into a chemical or physical signal with a well-established sensitivity and to supply high selectiveness to the aim molecule in the attendance of potentially interfering compositions [12]. The other functional unit of a chemical sensor is the physico-chemical transducer. Considering the transducer type, sensors could be categorized as optical, calorimetric, piezoelectric, and electrochemical [15,16].

Electrochemical sensors include the sensitivity benefit, a significant feature of electroanalytical approaches, that could be composed with receptor selectivity. As regards electrochemical biosensors, the biocomponent identifies its supplementary analyte leading to a catalytic or binding event that eventually produces an electrical signal that is adequate to the analyte concentration and that could be observed via the transducer [17]. Several applications have been examined for electrochemical sensors and biosensors in biomedical [18-20], environmental [20-22], industrial [20], and agricultural [23] applications. The electrochemical sensors and biosensors sensitivity could be significantly modified by using diverse nanomaterials like graphene [24], carbon nanotubes, MXenes, and metal nanoparticles [25]. Since nanomaterials have a vital role in the electrochemical wearable sensor's expansion, a brief overview of the most significant kinds of nanomaterials utilized in their manufacturing will be briefly explained. Numerous extensive reviews [26-30] have been done on this subject, thus the only crucial aspects will be described in the following. Graphene is a two-dimensional nanomaterial combined of sp2 bonded carbon atoms, which shows outstanding attributes like high surface area and exceptional electrical and thermal conductivity [31-33]. Graphene is a broadly utilized nanomaterial in numerous sensor applications Due to these attributes [31,32], comprising in the expansion of the wearable sensor for wound infection biomarker monitoring [34]. Single-walled carbon nanotubes (SWCNT) are another kind of carbon-based nanomaterial used for sensor applications. SWCNT have been considered a one-dimensional(1D) form of carbon that has been shaped via 'rolling' graphene into a tube structure [33,35].

SWCNT comprises well chemical stability, strength, and electrochemical conductivity. They were used for electrode amendment for lactate recognition in order to increment electrode surface area and so to enhance sensitivity [36]. MXenes are a new category of two-dimensional(2D) conductive nanomaterials, included of carbides, nitrides, or carbonitrides of early transition elements. MXenes include numerous features which turn them attractive for the wearable sensor's design. They are extremely flexible and incorporate the high electrical conductivity of transition elements with the hydrophilic features of their external layer [37,38]. The extensive variety of nanomaterials that could be utilized in electrochemical sensor manufacturing, along with the inherent benefits of electrochemical sensors has certified them for applications in various fields, comprising wound monitoring, as indicated in Table 1.

Table 1: Instances of electrochemical wearable and disposable sensors for wound infection biomarker monitoring.

Detection	Analyte	Technique	Linear Range	LOD	Matrix
AMP	UA	C-SPE/PB/uricase/Chi on wound dressing	100–800 µM	NS	PBS
AMP	UA	Embroided ink coated/ uricase thread (on gauze)	0–800 µM	NS	Simulated wound fluid
POT	pH	C/PANI on Ecoflex substrate	4–10	-	Standard pH buffer solutions, emulated wounds
POT	pH	ITOE/PANI, can be attached to bandage + NFC probe	4–10	-	Emulated wound and emulate infected wound
POT	pH	C-SPE/PANI on PET film, attached to commercial transparent tape	4–10	-	Standard pH buffer solutions
POT	pH	C electrode on the commercial bandage	2–13	-	Acidic and alkaline solutions
EIS	pH	Screen-printed CuO NR on IDE	5–8.5	-	Buffer solution, DMEM
SWV	pH	Riboflavin/LIG/ polyimide	2–8	-	Buffer solution
AMP	UA	Screen-printed carbon/uricase on omniphobic paper	0.22–0.75 mM	0.2 mM	PBS
EIS	pH		5.5–8.5	-	Standard pH buffer solutions
DPV	pH	LGG/MXene/PANI	4–9	-	Artificial wound exudate
AMP	UA	LGG/MXene/uricase	50–1200 µM	50 µM	Artificial wound exudate
SWV	UA	CNT/PA	100–1000 µM	NS	Simulated wound fluid
	Pyo		0.10–100 µM	0.1 µM	Simulated wound fluid, bacteria culture media
SWV	UA	CUA	100–700 µM	1 ± 0.4 µM	PBS, simulated wound fluid
	Pyo		1–250 µM	1 ± 0.5 µM	PBS, Simulated wound fluid, bacteria culture
	Nitric oxide		1–100 µM	0.2 µM	PBS, simulated wound fluid, eukaryotic cell culture
AMP	Oxygen	AuE/Nafion/PDMS on wound dressing	58.5–178 [O2] %	NS	PBS
AMP	Lactate	AuE/PB/SWCNT/Chi/ LO/SWCNT/Chi on wound dressing	0.1–0.5 mM		PBS

SWV	TNF-α	AuE/AuNPs-GP/Apt-MB	0–2	NS	Spiked serum, mice wounds, wound exudate
			ng/mL		
	IL-6		0–30		
			ng/mL		
	IL-8		0–30		
			ng/mL		
	TGF-β1		0–150		
			pg/mL		
	Staph. aureus		0–1 × 109 CFU		
	pH	PANI/AuE	4–9		

Note: AMP—amperometry; POT—potentiometric; UA—uric acid; C-SPE—carbon screen-printed electrodes; PB—prussian blue; Chi—chitosan; NS—not specified; PBS—phosphate buffer saline; RFID—radio frequency identification; NFC—Near-Field Communication; PANi-EB—polyaniline emeraldine base; PANI—polyaniline; ITOE—indium tin oxide electrode; PET— polyethyleneterephtalate; EIS—electrochemical impedance spectroscopy; NR—nanorods; IDE—interdigitated electrodes; DMEM—Dulbecco's Modified Eagle Medium; SWV—squarewave voltammetry; LIG—laser-induced graphene; DPV—differential pulse voltammetry; LGG—laser guided graphene; Pyo—pyocyanin; CNT—carbon nanotube; PA—polyacrylamide; CUA—carbon ultramicroelectrode arrays; AuE—gold electrode; PDMS—polydimethylsiloxane; SWCNT—single-walled carbon nanotubes; LO—lactate oxidase; TNF-α—tumor necrosis factor α; IL-6—interleukin 6; IL-8—interleukin 8; TGF-β1—transforming growth factor-β1; AuNPs-GP—gold nanoparticles graphene nanocomposite; Apt—aptamer; MB—methylene blue; CFU—colony forming units.

Perspectives and Conclusion

In recent years, technology and smart gadgets have quickly turned into an integrated part of our daily life. Sensors for biological parameters like gait, heart rate, or hypertension have already been utilized in smartphones and commercial wearable devices. In this regard, it is natural to anticipate that wearable and smart sensors will begin a vital role to play in the personalized medicine future. The field of wound infection diagnosis and monitoring creates no exception to this overall tendency. By evaluating the changes in diverse biomarkers existing in the wound environment, wearable sensors for wound infection illustrate the devices next generation that could be utilized in the future for a more fast and more precise diagnosis of infected wounds. Several benefits both for the patient and for healthcare personnel could be provided by the expansion of the wearable sensor for wound infection biomarker monitoring. Wound environment changes continuous monitoring could increment patient comfort and adoption by reducing the requirement for traumatic bandage elimination for wound inspection. By decreasing disruption to the wound healing procedure, will also simplify faster healing of the wound. In order to effectively accomplish wearable sensors for wound monitoring, it is crucial to make sure the specified specifications of the sensors, like high sensitivity, biocompatibility, constancy, as well as autonomous functioning, and wireless data transition. The nanomaterials incorporation like carbon-based or metal-based nanoparticles could assist to increment sensor surface and sensitivity though their usage is still disputable since no related data about their long-term toxicity and biocompatibility exist at the present time. In the future, research requires to concentrate on the expansion of fully autonomous sensors, that make sure wireless information transfer and could function without the requirement for non-portable devices. This will make sure incremented adoption and feasibility of the expanded devices.

There are presently numerous restrictions concerning the miniaturization of potentiostats, optic probes, or batteries that have been needed for sensor functioning, but continuous effort has been being made in order to tackle these challenges. There are already promising examples of autonomous sensors in the article along with instances of sensors that could be modified to achieve these intended targets. For to wearable sensors to be utilized on a large scale, they require to be intuitive to utilize and suggest consequences that are simple to read and construe. In this framework, the smartphone's incorporation with specifically designed applications in sensor usage is of strong interest. Instances of devices that could yield a consequence via simply taking a photo of the sensor or that could suggest a bare-eye approximation of diverse parameters are particularly promising for the field of wound infection biomarker monitoring. In the future, one more path that requires to be brought into attention is the mixture of diagnostic and therapeutic plans into the same 'smart dressing'. Wound dressings that release medicine relying on the concentration of biomarkers existing in the wound environment are of considerable interest because of their capacity of delivering the material at precisely the correct time. To conclude, this contribution exhibits the recent developments in the field of wearable and disposable sensors for wound infection biomarker monitoring. Several latest instances of wearable and disposable sensors from the article are shown in Table 1.

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