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Smart wound dressings

Streszczenie. *Wraz z rozwojem mikro i nanotechnologii rosną oczekiwania związane z poprawą jakości życia i zdrowia. Jednym z obszarów rozwoju są zastosowania inżynierii materiałowej i elektrycznej do identyfikacji stanu zapalnego skóry. Autorzy pracy opisują wyniki analizy rozwiązań technologicznych występujących w literaturze. Przedstawiają rozwiązania dotyczące wytwarzania i aplikacji sensorów do weryfikacji rozwoju stanu zapalnego ran, a także wpływu zastosowania elektroterapii do przyspieszenia gojenia się ran.* ***(Inteligentne opatrunki medyczne)***

Abstract*. With the development of micro and nanotechnology, expectations related to improving the quality of life and health are growing. One area of development is the application of materials and electrical engineering to identify skin inflammation. The authors of the work describe the results of the analysis of technological solutions existing in the literature. They present solutions for the production and application of sensors to verify the development of wound inflammation, as well as the impact of using electrotherapy to accelerate wound healing.*

Słowa kluczowe: elektronika noszona; opatrunek medyczny, inteligentne tekstylia
Keywords: wearable electronics; smart dressings, smart textiles

Introduction

With the development of wearable electronics, monitoring human health and life is gaining great interest. Smart dressings are also developing in this trend. These are technological solutions which task is to monitor the state of wound healing, including the development of various types of pathogens. Measuring the impedance of sensors, the pH level of wound secretions, its humidity and temperature is intended to help in quick medical diagnosis and improve treatment [1,2]. Artificial intelligence and machine learning algorithms can be used for this purpose [3,4]

Technological solutions related to smart dressings include special materials based on smart polymers, nanolayers or peptides that have antibacterial properties or stimulate tissue regeneration. Smart dressings support the healing of even chronic wounds that are difficult to heal and require an individual approach.

Solutions for structures sensitive to the development of pathogens must be constructed on flexible substrates. The available solutions include material substrates (Fig. 1.A - 1D) and platforms (Fig. 1E - 1H) that have been developed for flexible biosensors. Material substrates include: (A) polymer, - measurement of glucose, Na^+, K^+ and temperature (B) textiles - measurement of hydration status, electrophysiological activity, pulse and oxygenation, (C) paper - used, among others, as electrodes for ECG and EEG and (D) composites. Platforms include: (E) epidermis, (F) nanomesh, (G) microneedles (H) microfluidics [5].

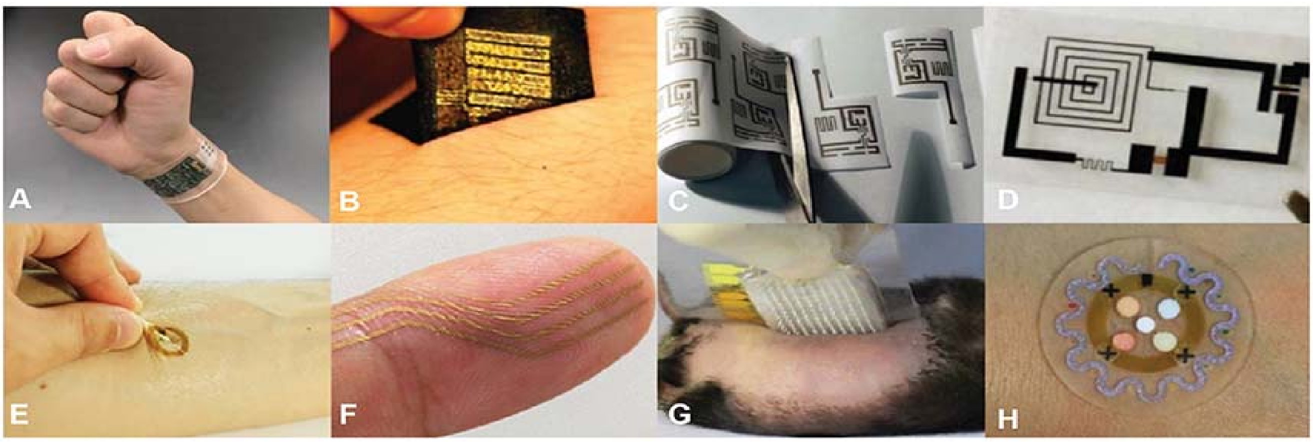

Figure 1. Material substrates (A–D) and platforms (E–H) that have been developed for flexible biosensors. (A) polymer, (B) textiles, (C) paper, (D) composites. The platforms include: (E) epidermis, (F) nanogrid, (G) microneedles (H) microfluidics. [5]

Modern solutions also help improve the quality of life of patients and may also reduce treatment costs.
However, the cost of producing such solutions, the possibility of intolerance of the chemical compounds used by the patient's skin, as well as possible specialized training in the use of the proposed solutions should be taken into account. However, solutions of this type should be treated as a form of treatment support, and the cost of production and use should be a marginal issue.

Exemplary solutions

Healthy human skin is covered with friendly and as well the harmful bacteria that quickly colonize an open wound. For this reason, wounds should be cleansed and antibiotic therapy performed in specific situations. Among the pathogens, one of the most dangerous is *Staphylococcus aureus* (*S.aureus*). So far, to detect the development of *Staphylococcus aureus*, medical staff observed the wound, took a swab from the infected area, and then analyzed the results of the laboratory test. However, swab tests are time-consuming, and swabs are performed at intervals when the condition of the wound is of concern to staff.

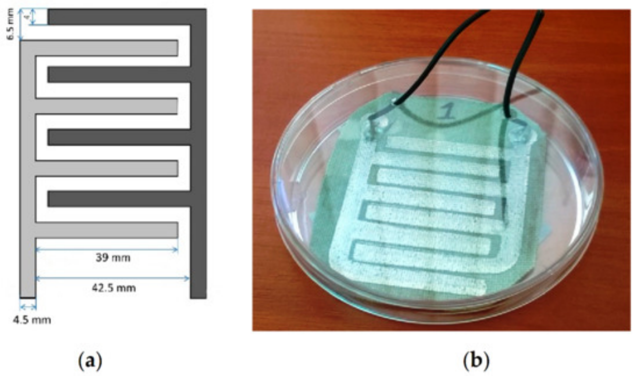

Figure 2. (a) Geometry of the fabricated metallic electrodes in the sensor enabling the detection of *Staphylococcus aureus*; (b) photo of the created structure [6,7]

To support the diagnosis of *Staphylococcus*, the authors of [6,7] proposed impedance sensors created on a textile composite substrate. In the process of physical vacuum deposition, silver electrically conductive layers in the shape of interdigitates electrodes were deposited on Cordura (Figure 2). The solution proposed by the authors enables the detection of the pathogen within approximately 10 hours from the moment the bacteria start multiplying in the wound. Measurements of the sensor's electrical parameters - electrical capacitance and resistance as a component of the real impedance were made using a CEM DT-9935 impedance meter for test frequencies of 100 Hz/120 Hz/1 kHz/10 kHz/100 kHz. The largest changes in capacitance, resistance and impedance over time were recorded for the test frequencies of 100 and 120 Hz [6,7].

Other research centers are also trying to develop devices that monitor signs of wound infection. According to Xiong's group, it is possible to detect wound inflammation by detecting an enzyme called deoxyribonuclease or DNase. The sensor detecting this enzyme uses the properties of a hydrogel, also called DNA gel. The sensor verifies the continuity of the gel's DNA chains and information about it is sent to appropriate systems identifying this change [8] (Figure 3).

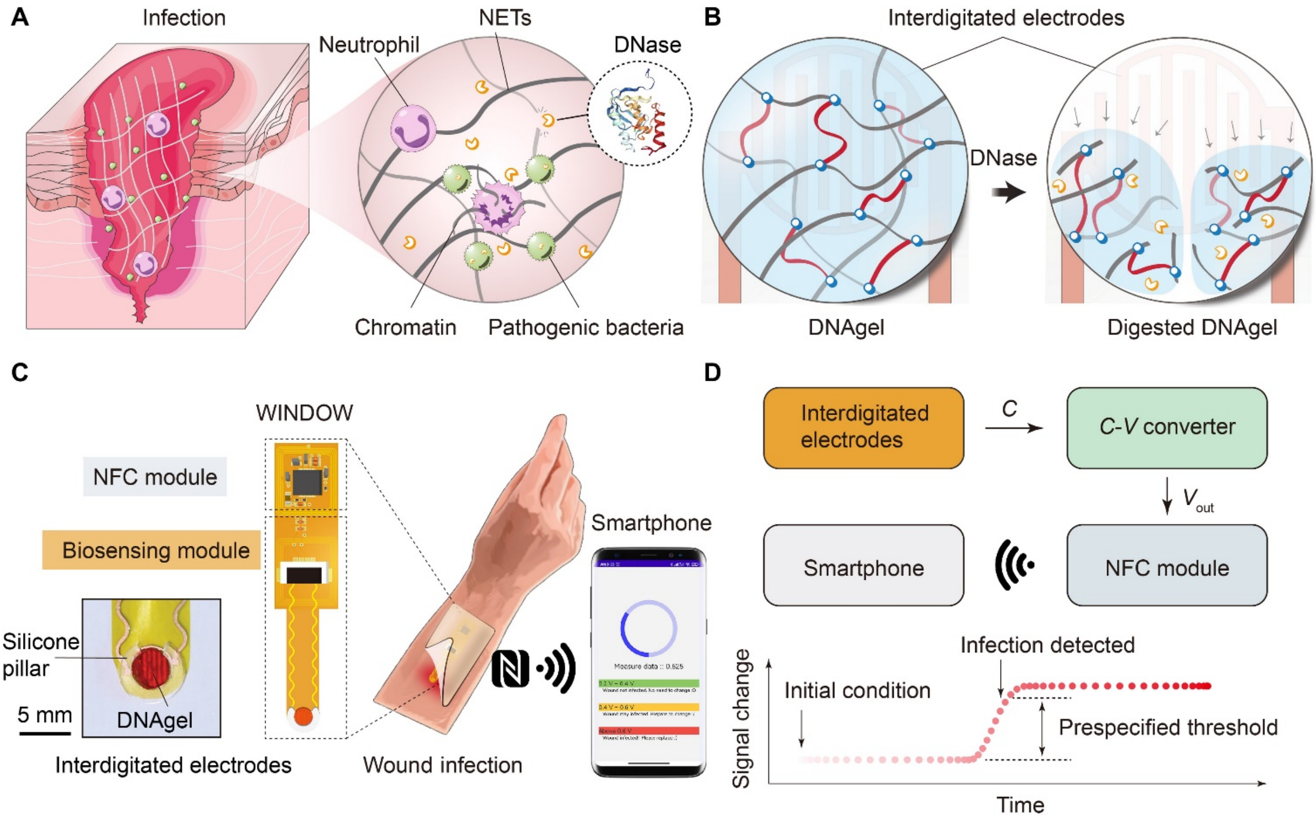

Figure 3. (A) Wound infections are made worse by DNase, a harmful substance that some bacteria produce. DNase helps bacteria escape from neutrophil extracellular traps (NETs), which are part of the body's defense system. (B) Diagram of how the infection is detected. The sensor has DNAgel, which is broken down by DNase, causing a change in the sensor's capacitance. (C) Diagram of the wireless device that monitors wound infection. WINDOW combines the DNAgel that reacts to infection, a biosensing module that uses half-wave–rectified LC, and an NFC module that allows a smartphone to read the wound condition. Inset image: DNAgel with sensor and rhodamine B dye. (D) Diagram of how the signal goes from the DNAgel-based biosensor to the NFC module and to a smartphone for wireless reading and display [8]

Smart dressings are expected to not only provide information on the physiological parameters of the wound, but also release substances that enhance skin regeneration. Mirani et al. [9] developed smart dual-sensor wound dressing for monitoring cutaneous wounds. For this purpose, they prepared beads which properties change depending on the glucose concentration. Glucose oxidase, horseradish peroxidase, potassium iodide, trehalose, which were dissolved in sodium citrate, were used for their production. Then, after washing with water and ethanol, they were placed in a glucose-sensitive solution, resulting in the formation of glucose-sensitive beads in the further process. After subsequent chemical processes, the material prepared in this way was used by the group to print hydrogel fibers, which were arranged into two-layer rectangular structures to create sensors. The developed product was incubated at specific temperatures in various media - pH sensors in buffers of known pH, and glucose sensors in glucose solutions of known concentrations. Then, an array of glucose and pH sensors were printed in a rectangular cavity, also placing drug-releasing ingredients in the mold. The dressings were sterilized with ultraviolet radiation for 45 minutes on each side.

Another solution which was developed by Xu et al [10], consists a two-layer bandage that can wirelessly send information about the changes in the measured values such the temperature, pH and uric acid levels in wounds. The developed system does not need a battery and can help detect bacterial infections early and using electric control can treat them fast with antibiotics [10]. The lower part of the bandage consists of a stretchable system of polyimide electrodes which can measure the pH and uric acid levels. Additionally, in the upper part, the temperature sensor and a flexible board for near-field communication (NFC) are placed. In this part of bandage, there is also a system which allows for supervision of the dose of drug given to the wound after connecting to a smartphone with NFC. Due to the implementation of various sensors in a small area and the ability to control the dose of the drug used at the same time, as well as battery-free systems, such solution may show the future trends in medical devices for wound treatment.

Among many technological solutions for creating skin-like structures [11] there are solutions combining rigid electronic sensors with elastomeric substrates. Their elastic properties are much weaker than solutions based on hydrogel, which are conductive skin sensors, Due to their high biocompatibility and high similarity of properties to physiological tissues, they have greater application potential. However, it should be noted that each type of used sensors, both gel-based and traditional sensors worn during their use, are exposed to mechanical damage, which impairs their long-term stability and reliability in monitoring and treating wounds. To prevent this type of effects, Khatib et al [12] proposed the use of self-healing materials that have the ability to self-repair without the need to use external stimuli, which increases the reliability in wound diagnosis. They developed an electronic skin that monitors temperature, pH and pressure (e-skin) with excellent self-healing ability. The proposed e-skin incorporates integrated sensors with self-healing polybutadiene-based poly(urea-urethane) (PBPUU) substrates [12].

Another solution for producing an e-skin dressing is the SmartHeal device built by a group of young Polish scientists [13]. This team of researchers used measurement of wound pH levels to monitor bacterial infection in wounds. For this purpose, a chemical sensor composed of graphene paste with ruthenium oxide and electroconductive paste with silver particles was used. The designed dressing assumes placing a chemical sensor with an RFID antenna between layers of sterile gauze.

Despite promising progress, smart dressing systems can most often monitor only one biomarker in a wound, which limits the accuracy of diagnosis and can lead to misleading treatment. Therefore, smart dressing systems that integrate multiple wound-related biomarker signal sensors are highly needed.

The wound healing process can be accelerated not only by using additional solutions that monitor the development of infection in the injured skin, but also by using impact of electromagnetic field [14] and electrotherapy. Thus, Rajendran et al. [15] conducted a literature review on the use of electrical stimulation (ES) to accelerate wound healing processes, taking into account its effectiveness in the healing of chronic wounds. The authors argue that a review of in vivo and in vitro studies shows that ES increases tissue perfusion, promotes cell migration, increases tissue vascularization and causes a significant improvement in fibroblast proliferation, which has a direct impact on the wound healing rate.

Electrical stimulation promotes the healing of chronic skin wounds such as diabetic ulcers and pressure sores. Researchers from South Dakota State University have developed a tool that predicts how cells migrate and arrange themselves under the influence of an electric field. They found that a weak electric field causes proteins on the cell surface to move to electric poles depending on their size and charge. It directs the cells to the center of the wound, where they form new tissue [16].

In another study on the effect of electric current on the acceleration of wound healing, Chu et al. [17] exposed the wounded skin of guinea pigs to a weak anodic direct current (DC) with an intensity of 20–40 μA to investigate its effect on the wound healing process. They found that wounds treated with DC had less granulation tissue and scar tissue than untreated wounds. In another experiment, Gürgen et al. [18] showed that the application of transcutaneous electrical nerve stimulation (TENS) to rat wounds resulted in a significant reduction in the level of pro-inflammatory cytokines in the wound tissue. They also noticed that the time needed for wound healing was shorter compared to the control group. Similar results have been obtained in other animal studies, which have shown that electrical stimulation (ES) increases fibroblast proliferation and collagen production in wounds, which promotes the remodeling phase of wound healing [19].

In chronic wounds in which there is excessive release of toxins and inflammatory signals, a reduction in the growth of at least one or all bacterial strains present in the wound has been reported following the use of electrical stimulation therapy [15]. Additionally, it was noticed that the use of a silver anode has a pronounced bacteriostatic effect under the influence of weak direct current compared to electrodes made of other materials. The explanation for this phenomenon is the formation of reactive oxygen species in this case. Pulsed current also promotes the reduction of bacteria due to the change in the pH of the bacterial environment. The current flow damages the outer membrane of the bacteria, allowing an uncontrolled influx of final solutes, allowing an uncontrolled influx of solutes that ultimately kills them [20].

Analysis of data presented on the basis of studies using high voltage pulsed current (HVPC) (80–330 V) compared to other types of current used in the case of electrotherapy for chronic wounds carried out by Khouri et al. [21] showed that when this type of current was used, the best results were achieved in reducing the size of chronic wounds.

In the case of electrical stimulation of wounds, positive results were also obtained using pulsed current (biphasic or monophasic waveform of value 1.2–1.5 mA which can be supplied to the tissue at high voltage), which penetrates deeper into the skin. This type of current does not cause skin changes, unlike direct current with constant amplitude, which causes skin irritation due to changes in pH [22]. Due to its polarization, the pulsed current may be similar to the physiological current compared to sinusoidal alternating current.

Discussion and conclusions

The authors focused on reviewing the developed solutions for the detection of pathogens developing on human skin, with particular emphasis on wounds. The described solutions concern sensors of one physiological parameter that can be detected using electrical measurements, and multi-sensor solutions used in one dressing are also indicated. The pursuit of the use of intelligent medical dressings is very justified due to the speed of medical diagnosis based on measurement results [23]. Additionally, attention should be paid to the wireless transmission of information using an electromagnetic field as a carrier of this information. Securing transmitted medical data, as well as clinical trials regarding developed prototypes, are also important legal and engineering issues.

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