Available *online* at : http://ejurnal.upnb.ac.id/

Jurnal Kesehatan

| ISSN (Print) 2085-7098 | ISSN (Online) 2657-1366 |

Healing Wound with Bioelectric Stimulation: A Systematic Review

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ARTICLE INFORMATION

Received: 01 July 2025
Revised: 15 July 2025
Accepted: 30 July 2025
Available online: 31 July 2025

KEYWORDS

Wound Healing, Bio electricity
Tissue engineering
Conductive materials, electrical stimulation

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ABSTRACT

Bioelectricity plays a critical role in cellular activities, guiding tissue repair and regeneration. In recent years, bioelectric stimulation has emerged as a promising therapeutic approach for chronic wounds that are resistant to conventional treatments. This review aims to analyze current research trends, mechanisms, and clinical applications of bioelectric stimulation in wound healing while identifying existing challenges and future research directions. A systematic literature review combined with bibliometric analysis was conducted using the Scopus database, identifying 831 open-access articles published between 2014 and 2024 with keywords related to “bioelectricity” and “wound healing.” Data were analyzed using VOSviewer to map research themes and trends. The analysis revealed three main research clusters: cellular mechanisms of bioelectric signaling, application of electrical stimulation for wound healing, and development of conductive biomaterials. Bioelectric interventions, including microcurrent stimulation and wearable bioelectric devices, were shown to accelerate wound closure, promote angiogenesis, and enhance tissue regeneration. However, variations in treatment protocols, lack of standardized parameters, and insufficient large-scale clinical evidence remain significant limitations. In conclusion, bioelectric stimulation demonstrates considerable potential to improve wound healing outcomes through enhanced cellular responses and tissue repair, and continued research is essential to develop standardized protocols, innovative bioelectric materials, and robust clinical evidence to support its clinical application

DOI: http://dx.doi.org/10.35730/jk.v16i2.1354

INTRODUCTION

The human body is inherently electrical. From the rhythmic contractions of the heart to the neural impulses that govern thoughts and actions, electrical signals orchestrate a complex symphony of life [1]. In recent years, harnessing this intrinsic bioelectricity has emerged as a promising frontier in medicine, particularly in wound healing. Chronic wounds, a global health challenge, often defy conventional treatments [2]. This literature review delves into the burgeoning field of bioelectronics, exploring its potential to revolutionize wound care. Systematically examining the existing research aims to elucidate the mechanisms underlying bioelectric stimulation, identify effective treatment parameters, and assess the clinical efficacy of bioelectronic interventions. Ultimately, this review seeks to contribute to developing innovative and productive therapeutic strategies for wound healing.

Despite the promising advances in bioelectric medicine, there remains a notable gap in the comprehensive understanding of its applications in wound healing. While preliminary studies have demonstrated potential benefits, the variability in experimental designs, treatment protocols, and patient outcomes highlights the need for a more unified approach [3]. Moreover, bioelectric therapies' long-term effects and safety are not yet fully understood. This gap underscores the importance of conducting rigorous, large-scale studies to establish standardized guidelines and optimize therapeutic outcomes.

Bioelectricity, the flow of electrical currents carried by mobile charged ions, plays a crucial role in the repair process of injured tissue [4]. This phenomenon is not limited to animals and humans; it also occurs in plants, influencing growth and development. The systematic review highlights the ubiquity of bioelectric characteristics across various species, emphasizing the importance of understanding these processes for regenerative therapies. The review underscores the need for further research on the mechanistic basis of bioelectricity in wound healing and regeneration, mainly focusing on mapping voltage patterns and the processes generating them [3].

Clinical studies have demonstrated the effectiveness of electrical stimulation (ES) in enhancing wound healing. Eviewed 15 high-quality studies on low-frequency ES and found that it significantly accelerates wound healing, with a 40% increase in wound area reduction over four weeks. This evidence supports the application of ES as a robust therapy for promoting wound healing, especially in cases where the natural repair mechanism is impaired.

Microcurrent stimulation (MCS), a form of ES, has been shown to facilitate biomolecular processes involved in wound healing and tissue repair. The parameters of MCS, including waveform shape, current type, polarity, amplitude, frequency, and pulse duration, are critical in optimizing its therapeutic effects. MCS has been demonstrated to mediate angiogenesis, reduce inflammation, and promote wound healing through various biomolecular responses [5]. In vitro models have also been used to study the bioelectric modulation of wound healing. These models comprehensively characterize the cellular, biochemical, biomechanical, and bioelectrical components involved in wound repair, which are essential for developing effective bioelectric strategies to control cell functions for improved bone regeneration [6]. The role of bioelectricity in directional cell migration during wound healing is another area of significant research. Studies have shown that epithelial cells and other cells involved in wound healing respond to electric signals, which are crucial in guiding cell migration and tissue repair [7].

The literature review highlights the critical role of bioelectricity in wound healing and regeneration across various species. Applying electrical stimulation, particularly microcurrent stimulation, has been demonstrated to be effective in promoting wound healing. Further research is needed to fully understand bioelectricity's mechanistic basis and develop more effective bioelectric strategies for regenerative therapies [3].

The role of bioelectricity in wound healing has garnered significant attention in recent years, with a growing body of research highlighting its crucial contributions to the healing process [8]. Bioelectricity refers to the flow of electrical currents carried by mobile charged ions across cell membranes and along the cells' exterior and interior ionic environment [4]. This phenomenon is essential for growth and development and is pivotal in wound healing and regeneration across various species, including animals, humans, and plants.

This literature review aims to summarize the existing knowledge on the nature, sources, and transmission of bioelectric signals involved in wound healing. It will explore how bioelectricity influences wound healing, including endogenous voltage gradients' role, exogenous electrical stimulation's impact, and physiological responses such as inflammation management, angiogenesis, and cell migration [2], [9]. Additionally, it will discuss the clinical applications and future research directions in bioelectrical stimulation for wound care.

This review will employ a bibliometric and literature review approach to address these gaps. By analyzing publication trends, citation networks, and research hotspots, the Researcer will map the landscape of bioelectric research in wound healing. This bibliometric analysis will provide insights into the field's most influential studies, key researchers, and emerging themes. Complementarily, a detailed literature review will synthesize the findings of individual studies, offering a cohesive narrative of the current state of bioelectric wound healing research. This research aims to highlight critical knowledge gaps and propose future research directions, ultimately advancing the field toward more effective clinical applications.

RESEARCH METHODOLOGY

This literature review aims to thoroughly explore the role of bioelectricity in wound healing through a systematic analysis of peer-reviewed studies. The research used the Scopus database to conduct a detailed literature search, ensuring that the sources were relevant and up to date. Bibliometric analysis was also applied to provide a clear, quantitative picture of the research landscape. The search focused on original research articles written in English, available as open access, and published between 2014 and 2024. Keywords such as “bioelectric,” “wound healing,” and related terms were used. The search was performed using the TITLE-ABS-KEY field so that only articles containing these keywords in the title, abstract, or author keywords were included. The search criteria were: publication year 2014–2024 (PUBYEAR > 2013 AND PUBYEAR < 2025), document type scientific article (LIMIT-TO (DOCTYPE, "ar")), language English (LIMIT-TO (LANGUAGE, "English")), and access open access (LIMIT-TO (OA, "all")). As a result, 831 scientific articles were identified. These articles were then analyzed using bibliometric and systematic approaches to identify research trends, main themes, and the contributions of bioelectricity to the wound healing process.Extracted data, including author names, titles, keywords, abstracts, and publication years, were imported into VOSviewer for analysis. Keyword co-occurrence maps were generated to identify research themes and trends. While VOSviewer provides a valuable tool for visualization, it is essential to acknowledge potential limitations in data scope and subjective interpretation of results. The articles found were 831 articles. The ten articles with the highest citation will discuss the research focus on bioelectric wound healing.

RESULT

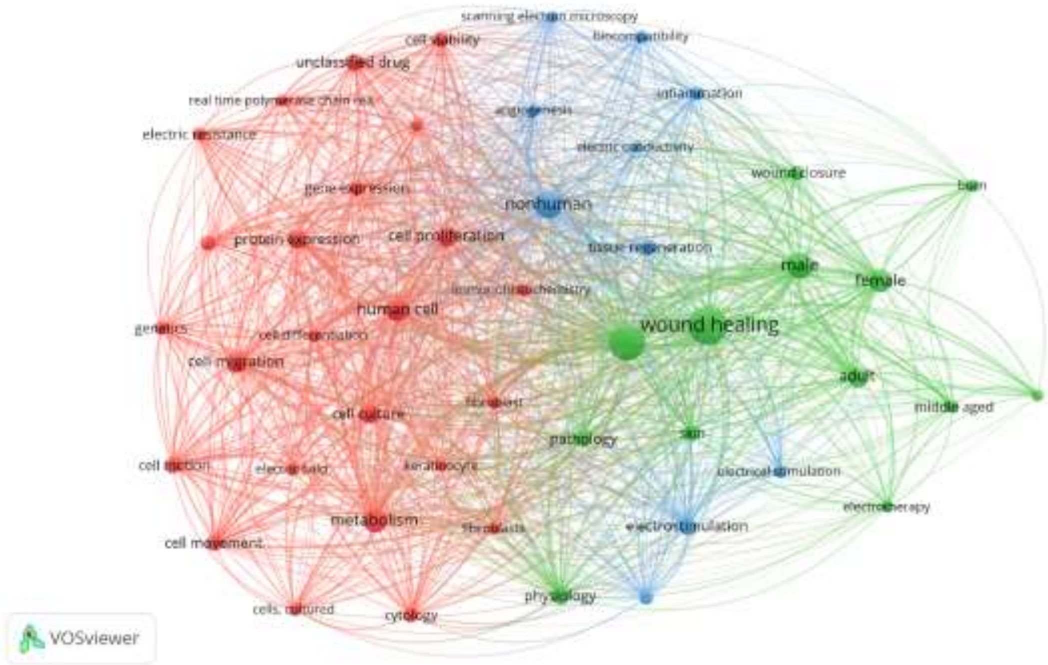

Figure 1. Co-occurrence of keywords

In this result, many articles focus on wound healing and made 3 Cluster. Cluster 1 focuses on wound healing. Cluster 2 focuses on bioelectric or electric, and Cluster 3 focuses on how to maximize

Table 1. Cluster 1

Keyword	**Occurrences**	**total link strength**
cell culture	138	2009
cell differentiation	65	1097
cell migration	164	2610
cell motion	101	1722
cell movement	102	1727
cell proliferation	153	2502
cell viability	87	1383
cells, cultured	64	1120
Cytology	88	1383
electric field	62	793
electric resistance	72	1099
electrical stimulation	62	724
enzyme linked immunosorbent assay	52	912
Fibroblast	55	953
Fibroblasts	50	746
gene expression	82	1430
Genetics	70	1308
human cell	199	3233
immunohistochemistry	65	1196
Keratinocyte	53	803
Metabolism	211	3519

Keyword	Occurrences	total link strength
protein expression	129	2291
real time polymerase chain reaction	53	1004
signal transduction	86	1419
unclassified drug	112	1888

The VOSviewer analysis of the provided data reveals a comprehensive research landscape focused on cellular processes and methodologies in bioelectricity and wound healing. Key areas of interest include cellular activities such as cell migration, proliferation, and viability, which are crucial for wound healing. Cell migration, with the highest occurrences and link strength, significantly focuses on how cells move to the wound site to initiate repair. Similarly, research on cell proliferation and viability highlights the importance of understanding how cells multiply and survive during healing.

Experimental techniques such as cell culture and enzyme-linked immunosorbent assays (ELISA) are prominently featured, indicating their critical role in studying cellular behaviours under controlled conditions and quantifying proteins involved in wound healing. Real-time polymerase chain reaction (PCR) is also emphasized for its utility in analyzing gene expression levels, which is essential for understanding the regulation of genes during the healing process. There is a notable interest in the effects of electrical stimulation and electric fields on cellular activities, suggesting a growing area of research in bioelectricity for wound healing. Keywords like the electric field, electrical stimulation, and electric resistance reflect efforts to explore how electrical forces can influence cell behaviour and improve healing outcomes. Specific cell types such as fibroblasts and keratinocytes are also central to this research, as these cells play crucial roles in tissue repair and re-epithelialization, respectively. The focus on protein expression further underscores the importance of identifying and understanding the proteins involved in the healing process and their regulation.

Broad biological processes like metabolism, gene expression, and signal transduction are also highlighted, indicating a significant interest in the underlying mechanisms of wound healing. Metabolism has the highest link strength, suggesting extensive research into metabolic processes during healing. The emphasis on gene expression and genetics highlights the importance of genetic studies in uncovering the molecular mechanisms driving wound healing. Overall, this analysis provides a detailed view of the interconnected research themes in cellular processes and bioelectricity, highlighting critical focus areas and potential directions for future research in wound healing therapies.

Table 2. Cluster 2

Keyword	occurrences	total link strength
Adult	162	2163
Burn	63	618
electrotherapy	55	693
Female	204	2672
Human	482	6072
Male	253	3496
middle aged	71	953
Pathology	109	1734
Physiology	126	1865
Skin	76	1051
treatment outcome	57	648
wound closure	77	969
wound healing	553	6135

The provided table offers insights into the research landscape of wound healing, as analyzed using VOSviewer. VOSviewer helps visualize and identify related keyword clusters, revealing the interconnections and focus areas within the field. In this table, the keywords are associated with occurrences and total link strength, indicating their prevalence and the strength of their connections to other keywords in the dataset. The keyword "Human" stands out with the highest occurrences (482) and total link strength (6072), signifying that a substantial portion of the research is focused on human subjects. This indicates a broad interest in understanding wound healing mechanisms and developing treatments applicable to humans. "Wound Healing," with 553 occurrences and a link strength of 6135, is the central theme of the research, as expected. It connects strongly with various other keywords, illustrating the multifaceted nature of wound healing research. Closely related is "Wound Closure" (77 occurrences, 969 link strength), highlighting specific interest in closing wounds as part of the overall healing process.

The demographics of research subjects are evident in keywords like "Female" (204 occurrences, 2672 link strength), "Male" (253 occurrences, 3496 link strength), "Adult" (162 occurrences, 2163 link strength), and "Middle Aged" (71 occurrences, 953 link strength). These keywords suggest a diverse range of study populations, with notable research focusing on gender differences and age-specific responses in wound healing. Keywords such as "Pathology" (109 occurrences, 1734 link strength) and "Physiology" (126 occurrences, 1865 link strength) emphasize the scientific investigation into the underlying mechanisms of wound healing. Understanding the pathological and physiological aspects is crucial for developing effective treatments. The keyword "Burn" (63 occurrences, 618 link strength) indicates a specific interest in studying wound healing in the context of burn injuries. Burns presents unique challenges in wound care, and research in this area aims to address these challenges. "Electrotherapy" (55 occurrences, 693 link strength) points to exploring electrical stimulation techniques as a treatment modality for enhancing wound healing. This aligns with the growing interest in bioelectric approaches to improve clinical outcomes. Finally, "Treatment Outcome" (57 occurrences, 648 link strength) underscores the importance of evaluating the effectiveness of various wound healing interventions. Research in this area aims to determine the best practices and therapies for achieving optimal healing results.

The VOSviewer analysis reveals a comprehensive and interconnected research landscape in wound healing, focusing on human subjects, diverse populations, underlying mechanisms, specific injury types, innovative treatments, and clinical outcomes. The research landscape in wound healing is extensive and multifaceted. The core focus is on understanding the wound healing process itself, including the mechanics of wound closure. Research delves into the physiological and pathological underpinnings of healing to develop effective treatments. A significant aspect of the research involves studying diverse populations, including differences based on gender and age.

Additionally, specific wound types, such as burns, are areas of concentrated study due to their unique challenges. There is a growing interest in exploring innovative therapeutic approaches, particularly electrotherapy, to enhance wound healing outcomes. Ultimately, the research emphasizes the importance of evaluating the effectiveness of different treatments to determine optimal care strategies. The study aims to understand wound healing comprehensively, identify factors influencing healing outcomes, and develop targeted interventions to improve patient care.

Table 3. Cluster 3

Keyword	occurrences	total link strength
angiogenesis	55	931
biocompatibility	65	806
electric conductivity	50	645
electric stimulation	67	952
electrostimulation	116	1606
inflammation	68	956
Nonhuman	291	4492
scanning electron microscopy	51	723
tissue regeneration	86	1021

In cluster 3, the provided data table highlights significant research themes and their interconnections as analyzed using VOSviewer. VOSviewer allows for the visualization and clustering of keywords, indicating prominent areas of study and their relationships. The keyword "Nonhuman" has the highest occurrences and total link strength, suggesting extensive research involving nonhuman models to understand bioelectric mechanisms before human applications. "Electrostimulation," with its high occurrence and link strength, emerges as a primary method studied for bioelectric interventions, focusing on applying electrical currents to wound sites to enhance cellular activities crucial for healing. Keywords like "Tissue Regeneration" and "Inflammation" indicate substantial research into how bioelectricity aids in regenerating tissues and modulating inflammatory responses to create an optimal healing environment. "Angiogenesis" and "Biocompatibility" are also prominent features, emphasizing the role of new blood vessel formation and the need for safe, compatible bioelectric devices in medical treatments. This analysis underscores the interconnectedness of these themes, highlighting how bioelectricity can be harnessed to improve wound healing processes through innovative medical approaches.

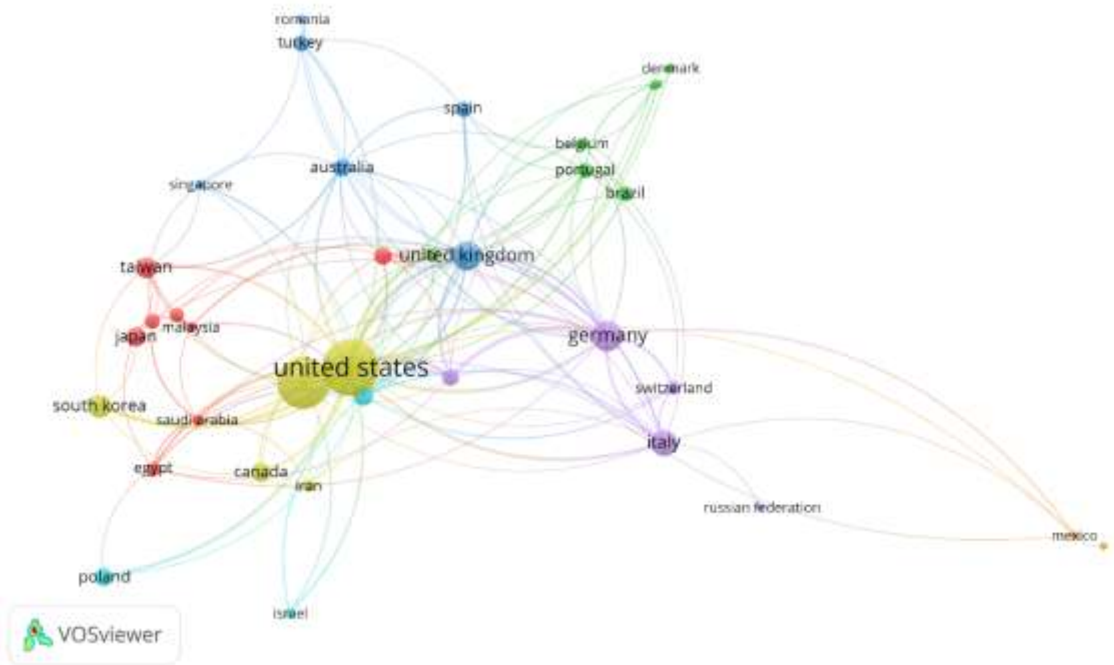

Figure 2. Citation by country

A bibliometric analysis using Vosviewer has revealed that the United States, Germany, the United Kingdom, and Italy are the leading countries in research focused on healing with bioelectricity. This indicates that these nations are at the forefront of exploring the therapeutic applications of electrical currents and fields, suggesting a strong emphasis on interdisciplinary collaborations and technological advancements in biomedical research.

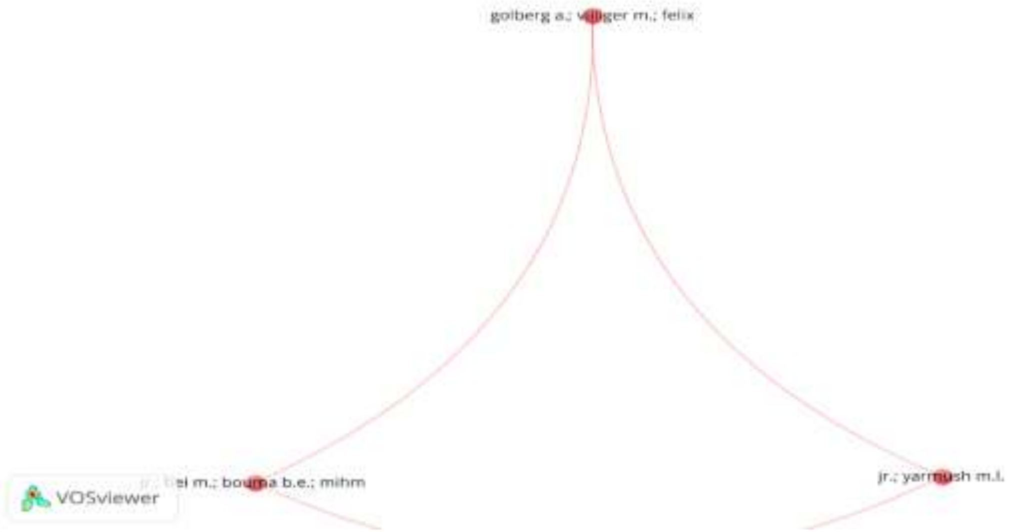

Figure 3. Co-occurrence of author keywords

831 Articles and only three authors have linked to the other.

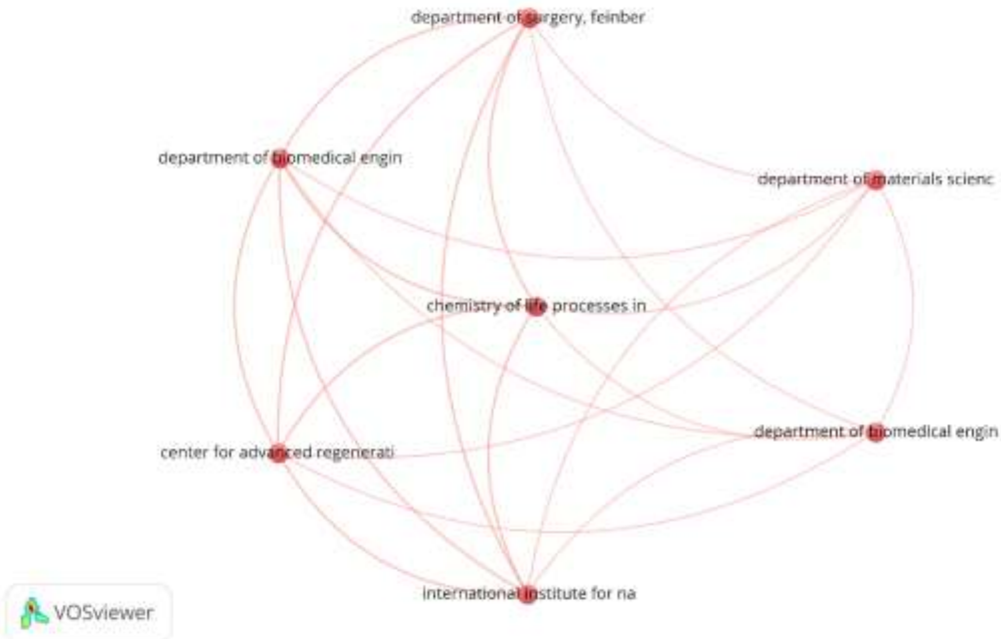

Figure 4. Co-occurrence of organizations

Only seven organizations have linked to other organizations. The strength of the link between two or more organizations can be indicated by the thickness of the line connecting them in the visualization. It concludes by identifying the seven most collaborative organizations.

Table 4. Ten Most Citations Article

No	Title	Result	Year	Citation
1	Conducting Polymers for Tissue Engineering	Conductive polymers like polyaniline, polypyrrole, and polythiophene have the potential for tissue engineering due to their biocompatibility. It can serve as bioactive scaffolds that stimulate cell growth through electrical signals. However, their limitations in flexibility and processing led to the development of conductive polymer composites, combining them with biodegradable materials. This review focuses on these composites in various forms (films, nanofibers, hydrogels, scaffolds) and their applications in regenerating bone, muscle, nerve, heart, and wound tissues. The article explores how conductive polymers and their composites create materials that can help repair damaged tissues.	2018	606
2	Effective Wound Healing Enabled by Discrete Alternative Electric Fields from Wearable Nanogenerators	Healing skin wounds is a significant healthcare concern. Despite the long-known effectiveness of electric stimulations in promoting skin wound healing, their practical use is still hindered by cumbersome electrical systems. This study presents a fast-acting electrical bandage for speeding up the healing of skin wounds. The wearable nanogenerator creates an alternating electric field on the bandage by converting skin movements into electricity. In rat studies, a full-thickness skin wound closed in 3 days, much faster than the usual 12 days for healing in rodents. Electric field-assisted fibroblast movement, growth, and transdifferentiation were found to speed up skin wound healing in in vitro studies. This self-powered electric dressing could make it easier to treat nonhealing skin wounds.	2018	248
3	Ultra-conformal drawn-on-skin electronics for multifunctional motion artifact-free sensing and point-of-care treatment	Current wearable bioelectronics often suffer from inaccuracies due to movement. To address this, researchers have developed a new type of electronics that can be directly drawn onto the skin. These drawn-on-skin electronics are highly conformable, customizable, and firmly adhere to the skin, making them resistant to movement artefacts. It can be used to create various devices for monitoring physiological signals, such as heart rate and brain activity, without being affected by body movement. Additionally, these electronics can be employed for electrical stimulation to accelerate wound healing. This technology offers a promising solution for accurate and reliable health monitoring and treatment by developing highly adaptable and practical skin-based electronics.	2020	210

No	Title	Result	Year	Citation
4	Electric cell-substrate impedance sensing for the quantification of endothelial proliferation, barrier function, and motility	ECIS is a technology that measures changes in electrical impedance to monitor cell behaviour. Researchers can track cell attachment, growth, and movement by applying a small alternating current to cells grown on electrodes. This non-invasive method provides real-time data without the need for labels or dyes. While ECIS is easy to use, understanding its complex theory is crucial for accurate data interpretation. While a detailed protocol is lacking, existing guidance covers cell attachment, growth, barrier formation, migration, and wound healing. Results from specific cell types (MVEC, HUVEC) can be applied to other adherent cell types.	2014	187
5	3D Printed Functional and Biological Materials on Moving Freeform Surfaces	Traditional 3D printing techniques usually use open-loop, calibrate-before-printing operations. Adaptive 3D printing is a different method that uses real-time feedback control and direct ink writing of functional materials to create devices on moving freeform surfaces. An integrated robotic system with computer vision can perceive changes in the geometries and motions of target surfaces in the 3D printing workspace. By combining 3D printing of electrical connections with automatic placement of surface-mounted electronic components, functional electronic devices can be created on a human hand that can move freely. Cell-filled hydrogels are printed on live mice using the same method, serving as a model for studying wound-healing diseases in the future. This 3D printing method could bring about new intelligent manufacturing technologies for directly printing wearable devices on the body and for advanced medical treatments.	2018	166
6	Stretchable, dynamic covalent polymers for soft, long-lived, bioresorbable electronic stimulators designed to facilitate neuromuscular regeneration	Bioresorbable electronic stimulators are gaining popularity as therapeutic platforms for bioelectronic medicines, treating diseases, speeding up wound healing, and eliminating infections. Researchers are introducing advanced materials that can operate in these systems for long periods and safely break down into harmless products, eliminating the need for surgical removal. The devices use a bioresorbable dynamic covalent polymer as a soft, elastic substrate and coating for wireless electronic components. Researchers discuss the key features, chemical design considerations, and polymer biocompatibility. These polymers enable stable, long-term wireless operation, demonstrating the potential for long-term electrical stimulation in enhancing muscle receptivity and functional recovery in a rat model of peripheral nerve injuries.	2020	162

No	Title	Result	Year	Citation
7	Effectiveness of interventions to enhance healing of chronic ulcers of the foot in diabetes: A systematic review	The International Working Group of the Diabetic Foot (IWGDF) has published a review of studies on improving chronic ulcer healing from 2010 to 2014. The review included ten categories and found limited evidence supporting newer therapies, except for negative pressure wound therapy in post-operative wounds. The diversity of studies made it impossible to combine results for analysis. The review concludes that the best treatment for diabetic foot ulcers remains uncertain.	2016	149
8	A Fully Biodegradable Battery for Self-Powered Transient Implants	Biodegradable transient devices could be crucial in wound healing and tissue regeneration. However, wired external power or wireless energy harvesters limit their electrical stimulation and sensing functions. This article presents a fully biodegradable magnesium-molybdenum trioxide battery as a potential power source for in vivo use. The battery provides stable, high output voltage and long lifespan, meeting implantable electronics needs. It is biodegradable and shows good biocompatibility, offering a promising solution for self-powered bioresorbable implants and eco-friendly electronics.	2018	142
9	Human Adipose-Derived Stem Cell Conditioned Media and Exosomes Containing MALAT1 Promote Human Dermal Fibroblast Migration and Ischemic Wound Healing	The study found that ADSCs release tiny particles called exosomes containing genetic material like lncRNA MALAT1. These exosomes promote cell migration and wound closure. By applying exosomes directly to wounds, without using the actual stem cells, researchers could speed up healing in both laboratory tests and animal models. This approach offers a potential new treatment for chronic wounds.	2018	130
10	Angiogenesis is induced, and wound size is reduced by electrical stimulation in an acute wound healing model in human skin	The study found that applying electricity to wounds promotes new blood vessel growth (angiogenesis). This process helps wounds heal faster and better. Using ES, researchers observed faster wound closure, increased blood flow, and higher levels of growth factors (VEGF-A and PLGF) compared to wounds without ES. These findings suggest ES could be a valuable treatment for slow-healing or chronic wounds.	2015	111

Conductive polymers show potential for tissue engineering because they are biocompatible and can interact with biological systems. These materials can make scaffolds that imitate the natural tissue environment, supporting cell growth and differentiation. These scaffolds can also provide electrical stimulation, which improves tissue regeneration by including conductive properties [10].

Research has demonstrated that using electricity to stimulate wounds can speed up healing [2]. Creating wearable nanogenerators to convert skin movements into electricity shows potential for delivering this stimulation. Furthermore, conductive inks can be used to make flexible electronic devices on the skin, allowing for real-time monitoring of wound healing and targeted electrical therapies [11]. Another focus area is creating biodegradable electronic devices for medical use. These devices can provide electrical stimulation or detect physiological signals without surgery [10]. Researchers aim to develop implantable devices that can safely degrade after use using biocompatible materials.

Incorporating conductive polymers and electronic components into tissue engineering has great potential to improve wound healing, tissue regeneration, and medical treatments [12]. Despite remaining challenges, such as creating dependable power sources for implantable devices, continuous research leads to new and creative solutions [13].

DISCUSSION

Based on the user's query, the mechanisms of bioelectric signalling in wound healing, the use of bioelectric approaches to enhance wound healing in clinical settings, the challenges and limitations of using bioelectric techniques in wound healing, and the potential applications of bioelectric technology in tissue regeneration and wound healing.

The Intersection of Conductive Materials and Tissue Engineering

The field of tissue engineering has witnessed significant advancements with the integration of conductive materials. Polymers like polyaniline, polypyrrole, and polythiophene, renowned for their biocompatibility, have been widely applied in bioactuators, biosensors, neural implants, drug delivery systems, and tissue engineering scaffolds [14]. These conductive polymers offer the potential to create bioactive scaffolds capable of stimulating cell growth and tissue regeneration through electrical signals. However, their inherent limitations in flexibility and processing have spurred the development of conductive polymeric composites, combining them with biodegradable polymers to enhance their suitability for tissue engineering applications. Various conductive biomaterials, including films, nanofibers, hydrogels, and scaffolds, have been fabricated using electrospinning, coating, and in situ polymerization techniques. These materials have shown promise in regenerating bone, muscle, nerve, and heart tissue and promoting wound healing [15].

In wound healing, the therapeutic benefits of electrical stimulation have long been recognized [15]. Recent innovations have led to the development of wearable nanogenerators that convert skin movement into electricity, creating an electrical field to accelerate wound closure [16]. The emergence of drawn-on-skin electronics offers customizable, conformable, and robust platforms for delivering electrical stimulation and monitoring wound healing.

The behaviour of cells in culture can be meticulously studied using Electrical Cell Impedance Sensing (ECIS). Researchers can gain insights into cell attachment, growth, morphology, and function by measuring changes in electrical impedance [17]. While the ECIS technique is valuable, its complexity and lack of standardized protocols have hindered its widespread adoption [18]. Nonetheless, available guidelines provide a framework for studying cell behaviour and wound healing processes.

The quest for self-sufficient implantable devices has led to the development of biodegradable electronic stimulators. These devices, powered by innovative magnesium-molybdenum trioxide batteries, offer the potential for long-term electrical stimulation without the need for surgical removal. Such advancements are crucial for addressing chronic conditions and enhancing tissue regeneration [12]. Furthermore, the role of stem cells and their derived extracellular vesicles (exosomes) in wound healing has garnered attention. Exosomes containing genetic material, like lncRNA MALAT1, have been shown to promote cell migration and wound closure [17]. Their application holds promise as a novel treatment for chronic wounds.

The convergence of materials science, electronics, and biology has yielded remarkable advancements in tissue engineering and wound healing. Conductive polymers, wearable electronics, and biodegradable devices are at the forefront of these developments, offering new possibilities for therapeutic interventions. While challenges persist, ongoing research and innovation are poised to transform the landscape of regenerative medicine [15], [19].

Mechanisms of Bioelectric Signaling in Wound Healing

Bioelectricity plays a vital role in wound healing, as the endogenous electric field guides cell migration and stimulates the secretion of growth factors [4]. External electric stimuli have been shown to significantly positively influence wound healing, although the exact mechanism remains unclear [8]. A 'healing-on-chip' approach has demonstrated that electrical stimulation can accelerate wound healing by closing a gap between layers of skin keratinocytes twice as quickly as unstimulated tissue [9].

Use of Bioelectric Approaches to Enhance Wound Healing in Clinical Settings

Studies have shown that applied electric fields can accelerate wound healing by providing directional signals for cell migration toward the wound centre [2]. A bioelectric dressing has been demonstrated to expedite acute wound healing, with faster epithelialization and improved scar appearance compared to standard dressings [20]. Low-level microcurrents from a bioelectric wound care device have promoted enhanced healing rates and improved aesthetic outcomes in equine traumatic lower-extremity wounds [5][21].

Challenges and Limitations of Using Bioelectric Techniques in Wound Healing

The current selection of parameters for electric stimuli tends to be arbitrary or empirical, making it inefficient and ineffective [8]. Despite the potential of bioelectric technology, challenges, such as a lack of standardization between stimulation methods and electrode technology for device development, exist [9][22]. Novel wound dressings with inherent electric activity are emerging, but studies of these specific modalities are lacking, indicating a need for further research [20][23][24].

Potential Applications of Bioelectric Technology in Tissue Regeneration and Wound Healing

Combining electrical stimulation with tissue-engineering approaches offers a self-stimulated scaffold to heal skin wounds without using potentially toxic growth factors and exogenous cells. Integrating electrical stimulation with biodegradable self-charged piezoelectric nanofiber matrices has shown promise in promoting skin regeneration and preventing bacterial growth [6]. Nanogenerators designed for energy harvesting and converting mechanical energy into electrical power have emerged as a next-generation technology for accelerating wound healing [25].

CONCLUSION

Bioelectric signalling plays a crucial role in wound healing by guiding cell migration and stimulating growth factor secretion. While bioelectric approaches have shown promise in enhancing wound healing in clinical settings, challenges such as lack of standardization and arbitrary selection of parameters exist. However, the potential applications of bioelectric technology in tissue regeneration and wound healing, including the development of novel wound dressings and nanogenerators, offer exciting prospects for future research and clinical interventions.

AUTHOR CONTRIBUTION

Nuh Huda: Executed the systematic literature review for this research, conducted data extraction and analysis, and served as the principal author of the manuscript, Provided guidance during the research process, served as the corresponding author, and conducted a critical evaluation and refinement of the article. Imroatul Farida: Contributed to formulating the review methodology, provided qualitative and quantitative analysis knowledge, and engaged in the article review process. Ceria Nurhayati: Oversaw the review effort, ensured methodological rigor, and participated in the final editing and approval of the manuscript.

ACKNOWLEDGEMENT

The author would like to express his deepest gratitude and appreciation to the management of STIKES Hang Tuah Surabaya for their invaluable support and guidance during this research. Their expertise and encouragement have played a significant role in shaping the quality of this systematic literature review.

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