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REVIEW

Research Hotspots in Natural Products for Wound Healing: A Bibliometric Analysis and Literature Review

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Purpose: Wound healing is a common chronic disease that has gradually become a significant healthcare burden. The therapeutic potential of natural products in modulating pathological wound healing mechanisms has attracted increasing attention in recent years. A new focus in the field of promoting wound healing has emerged through the study of the mechanism of action of herbs and their derivatives and the translation of the results. This study aims to analyze and summarize the current status, research trends, and hotspots in this field to provide reference and direction for future research.

Methods: Literature related to wound healing and natural products in the Web of Science Core Collection was searched and collected. Bibliometric and visualization analyses were performed using Microsoft Excel 2021, bibliometric tools (VOSViewer, Citespace 6.3. R1, and bibliometrix R package), and R 4.3.2.

Results: A total of 2394 publications were included in this study. The annual number of publications has increased in this field year by year. China is the most productive country. Egyptian Knowledge Bank is the most influential research organization in terms of research output. AKKOL EK and LEUNG PC are the most influential authors in this field. *JOURNAL OF ETHNOPHARMACOLOGY, MOLECULES, PHYTOTHERAPY RESEARCH* are the most influential journals. Initially, research was focused on keywords such as medicinal plants, oxidative stress, inflammation, antimicrobial activity, and apoptosis. In recent years, new research hotspots have emerged, including pyroptosis, ferroptosis, collagen deposition, and nanodrug delivery.

Conclusion: The study of the relationship between natural products and wound healing has a promising future, and translational research targeting natural products will be the focus of future chronic wound therapy research.

Keywords: wound healing, herb, bibliometric analysis, visualization, VOSviewer, CiteSpace

Introduction

Skin serves as the body's primary defensive organ, with a wound defined as a disruption in the continuity of the skin.[1] The wound healing process comprises four stages: hemostasis, inflammation, cell proliferation, and tissue remodeling.[2,3] Wounds are clinically classified as acute or chronic. Acute wounds progress through a well-orchestrated healing cascade, facilitated by adequate blood supply and intact immune responses.[4] In contrast, chronic wounds fail to follow this sequential repair process, which may be related to underlying diseases, inflammatory infections, immune abnormalities, and oxidative stress, among others.[4–6] The treatment of wounds is crucial for human health. Failure of epidermal healing and prolonged treatment times not only increase the financial burden on patients but also have significant social consequences for healthcare providers and physicians, patients, and their families.[7,8] Patients experience frequent pain, limited mobility, excessive exudate, wound odor, and restricted social interactions,[9] which also indirectly increase the society and healthcare system's maintenance costs.[10] More

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than 8.2 million people in the US suffer from wounds, with care costs ranging from $28.1 billion to $96.8 billion. The global wound care market was valued at $18.4 billion in 2018 and is expected to grow at a compound annual growth rate (CAGR) of 3.9% from 2019 to 2026.[11] Globally, 1–2% of the population will develop chronic wounds,[12] with prevalence escalating due to aging populations and rising rates of diabetes, obesity, and vascular disorders.[13] Despite advances in wound care, evidence-based therapies for refractory chronic wounds remain limited, particularly in patients with multiple comorbidities.

Natural products are known to possess anti-inflammatory, antioxidant, angiogenesis-stimulating, and immune-modulating properties, which are crucial for wound healing. Compared to chemical drugs, herbal products offer enhanced safety profiles and cost-effectiveness, aligning with the growing demand for affordable wound therapies amid rising healthcare costs.[1] Natural products have a long history of use as therapeutic medicines dating back to ancient times. While many lack the evidence-based foundation of modern medicine, emerging research highlights the potential of these approaches in managing chronic diseases, including wound healing. Herbs consist of various parts of a plant, the herb itself, roots, stems, herbal extracts, and purified herbal monomers containing the main active ingredient. In India, a wide range of herbs, including turmeric, have been used since as early as 1900 BC.[14] Numerous chemicals derived from natural products or herbal remedies have been shown to aid in fighting inflammation and infection, as well as promoting wound healing. Therefore, natural products and their derivatives have advantages in the treatment of chronic wounds and have garnered significant attention from researchers. Studies have demonstrated that neem leaf extract can be used as an alternative to normal saline for irrigating foot ulcers and is safe for use.[15] Phenolic compounds in pomegranate peels have significant healing-promoting effects on wounds in experimental animals.[16] Electrospun Janus nanofibers promote wound healing by loading the active portion of a natural product into different polymer matrices.[17] Numerous published studies on the use of herbs and their derivatives in wound healing applications have been documented in the literature, highlighting the potential application of natural products in chronic wound treatment.

Bibliometric analysis is the systematic and orderly analysis of literature under defined conditions through relevant software tools, which helps to qualitatively and quantitatively analyze the attributes of scientific publications as well as research trends.[18,19] This method is used widely in the medical field research nowadays to get a quick overview of research trends and relevant hotspots and to assess the distribution of authors, countries/regions, and journals within the research area,[19–22] which helps to identify future research directions and developments. To explore the research of natural products in the field of wound healing, this study summarizes and visualizes the global situation, research hotspots, and trends through bibliometric analysis using tools such as CiteSpace, VOSviewer, and R (version 4.3.1). This study aims to summarize the current status and future trends in research on natural products, including herbs, in the field of wound healing. It explores the hotspots and evolutionary trends in this field, providing valuable references for researchers and expanding the methods of disease prevention, diagnosis, and treatment.[23]

Methods

Literature data were retrieved from the Web of Science Core Collection (WOSCC) database, which was published from January 1, 2001, to September 20, 2024. To ensure the comprehensiveness of the study, the search strategy employed the following formula: AND TOPIC = (“Wound Healing” OR “Healing Wound” OR “Wound Healings”) AND (“Herb” OR “Traditional Chinese Medicine” OR “Medicinal Plants” OR “Herbal Medicine” OR “Chinese Plant Extracts” OR “Herb Extracts” OR “Herbal Compounds” OR “Plant Compounds” OR “Phytochemicals” OR “herbal medication” OR “herbal medicine” OR “herbal formulas” OR “herbal extract” OR “herbal supplement” OR “herbal products” OR “traditional medicine” OR “traditional herbal medicine”). Relevant literature was exported and subsequently imported into the literature management tool for data cleaning and ranking, ensuring the accuracy and completeness of the final dataset. In the literature screening process, only articles, review articles, book chapters, and early access articles were included.

Results

Global Publications and Trends

The initial search identified 2440 articles, which were then filtered down to 2394 for final analysis. The number of annual publications on wound healing and research related to herbal medicine demonstrates a significant upward trend, with an

average yearly growth rate of 22.51% from 2001 to 2024 (Figure 1). Between 2001 and 2008, publication volumes remained relatively low. However, a gradual increase began in 2009, followed by accelerated growth after 2015. This surge resulted in 106 publications in 2016 and over 150 by 2019. Between 2020 and 2024, the annual number of publications exceeded 270, reaching a peak of 320 in 2024. The years 2022, 2023, and 2024 (as of mid-September) also recorded more than 300 publications. These trends suggest that research in this field entered a phase of rapid development after 2016, with exponential growth following 2020, reflecting a heightened academic interest in herbal medicine applications for wound healing.

Countries/Regions, Institutions, and Authors

From the perspective of global publication output across different countries, China led with 795 articles. Of these, 714 articles were attributed to single-country publications (SCP), while 81 articles were multiple-country publications (MCP), yielding an MCP ratio of 0.102 (Figure 2A and B). India ranked second (275 articles, MCP ratio = 0.229), followed by Iran (143 articles, MCP ratio = 0.175). Despite lower output volumes, South Korea and Turkey demonstrated strong international collaboration, with MCP ratios of 0.231 and 0.215, respectively.

In terms of total citations, China led with 14,098 total citations but had a lower average of 17.7 citations per article, likely due to its high publication volume (Figure 2C). By contrast, Italy (38 citations/article) and the United States (34.2 citations/article) achieved higher per-article influence despite smaller outputs. Overall, China dominates the research output in this field. Meanwhile, the United States plays a pivotal role in fostering international academic collaboration, with higher-quality research primarily originating from countries that frequently cooperate (Figure 2D).

The institutions with the highest publication output are concentrated in Egypt (Figure 3A). The Egyptian Knowledge Bank ranked first with 175 articles, highlighting its significant contribution to the field. Nanjing University of Chinese Medicine and China Medical University, Taiwan, ranked second and third with 118 and 100 articles respectively, reflecting their sustained high scientific output in the field. Additionally, the Chinese University of Hong Kong, Tehran University of Medical Sciences, Mashhad University of Medical Sciences, Islamic Azad University, Shahid Beheshti University of Medical Sciences, and Shanghai University of Traditional Chinese Medicine also contributed to

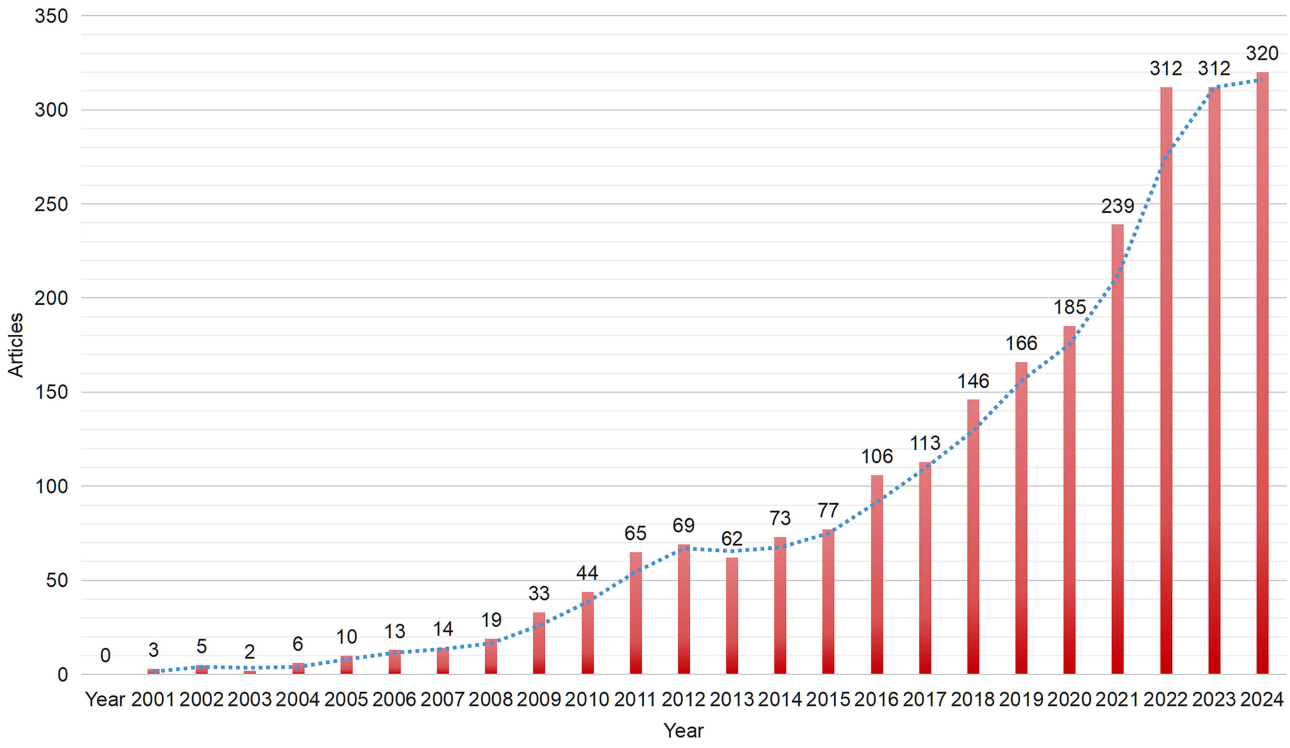

Figure 1 Global trends in the number of articles.

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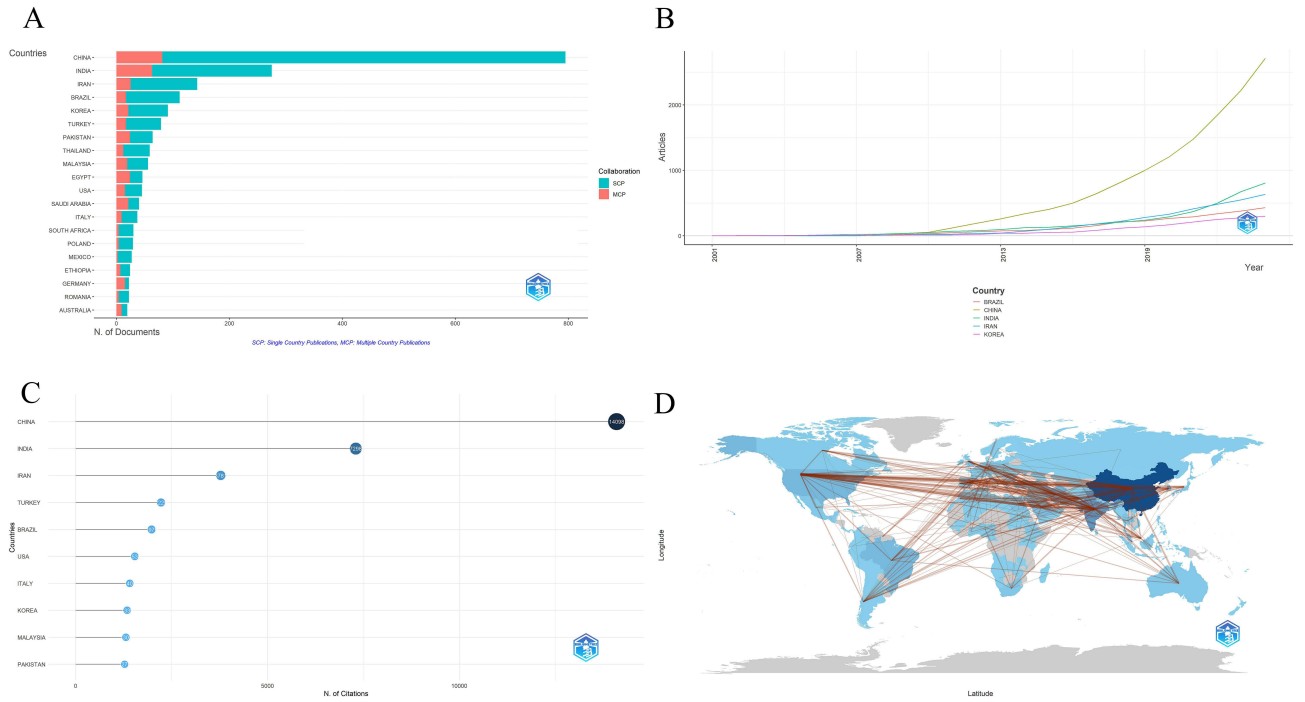

Figure 2 Visualization results of countries/regions: (**A**) Corresponding author's country; (**B**) Country production trends over time; (**C**) Top 10 countries with the most citations; (**D**) Map of country cooperation networks.

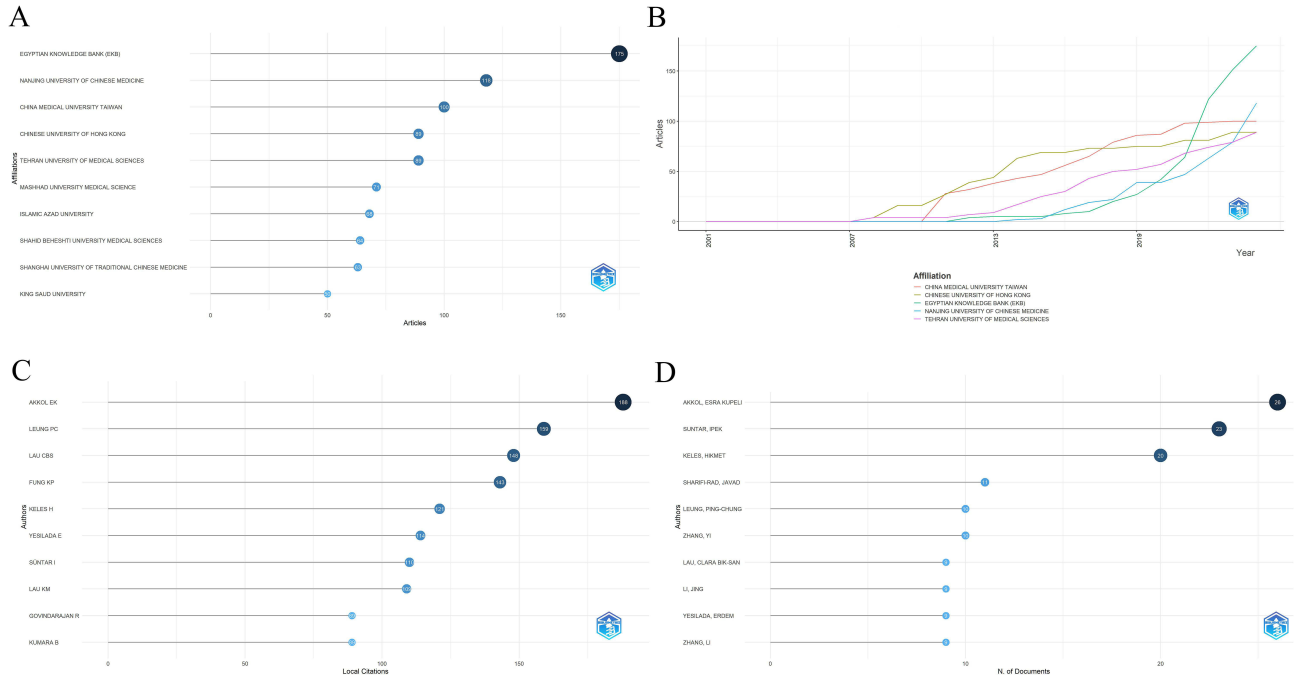

Figure 3 Visualization results of institutions and authors: (**A**) The most global prolific institutions; (**B**) Affiliations' production over time; (**C**) Most locally cited authors; (**D**) Most relevant authors.

the field. These data demonstrate the dominance of Chinese institutions in wound healing research, and the presence of international institutions from Egypt and Iran highlights the significant contribution of the Middle East to this field.

Before 2007, the Council of Scientific and Industrial Research (CSIR) in India had pioneered research in this field and gradually emerged as a prominent institution (Figure 3B). Since 2007, over a dozen institutions from China have begun

publishing research in this area. This explains why China leads the world in citation counts despite its later start. Among these institutions, Nanjing University of Traditional Chinese Medicine ranked second in terms of publication volume and exhibited the highest frequency of collaboration. King Saud University, situated in the Middle East, has also demonstrated significant influence and actively fosters cross-institutional partnerships.

A total of 11,836 authors contributed to this research domain. The most cited authors were AKKOL EK and LEUNG PC (Figure 3C), while AKKOL EK and SUNTAR IPEK emerged as the most relevant authors (Figure 3D). The author's collaboration analysis reveals a global distribution of researchers with established cooperative relationships, forming teams of considerable scale.

Journals/Cited Journals

A total of 631 journals have published research in this field. The most prolific journals included J*OURNAL OF ETHNOPHARMACOLOGY, EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE, MOLECULES, FRONTIERS IN PHARMACOLOGY*, and *PHYTOMEDICINE*. Among these, *JOURNAL OF ETHNOPHARMACOLOGY, MOLECULES*, and *PHYTOTHERAPY RESEARCH* were the most cited, representing the most influential journals in the field (Table 1).

Cited Articles

The top 10 most cited articles focused on ethnopharmacology, oxidative stress, inflammatory response, and complementary and alternative medicine (Table 2). The most cited article, "Phenylpropanoids as naturally occurring antioxidants: from plant defense to human health",[24] emphasized the role of phenylpropanoids in mediating cellular defense and their relevance to inflammation development and wound progression.

Research Hotspots

Keyword clustering revealed interconnected themes, including herbal extracts, apoptosis, oxidative stress, in vitro studies, and antimicrobial activity, forming a complex research network (Figure 4). Wound healing strongly correlated with medicinal plants, antioxidant activity, and extracts, highlighting natural products as the primary research focus (Figure 4A and B). The high correlation between in vitro studies, antimicrobial activity, and apoptosis suggested that the main direction of experimental validation focuses on functional evaluation and mechanistic exploration. Traditional medicine was linked to the extraction and separation of chemical compositions, indicating that research is moving

Table 1 Top 10 Most Productive Journals and Cited Journals

Rank	Journal	Count	Cited Journals	Times of cited
1	Journal of Ethnopharmacology	310	Journal of Ethnopharmacology	7785
2	Evidence-Based Complementary and Alternative Medicine	76	Molecules	2078
3	Molecules	74	Phytotherapy Research	1875
4	Frontiers in Pharmacology	60	Evidence-based Complementary and Alternative Medicine	1470
5	Phytomedicine	37	Phytochemistry	1436
6	South african Journal of Botany	35	Planta Medica	1307
7	Phytotherapy Research	32	Food Chemistry	1252
8	International Journal of Molecular Sciences	30	Plos one	1193
9	Biomedicine & Pharmacotherapy	29	International Journal of Molecular Sciences	1188
10	HELIYON	27	journal of Agriculturual and Food Chemistry	1176

Table 2 Top 10 Most Cited Articles

SCR	Author and Year	DOI	Title	Journal (IF-2023)	TC	TC per Year TC
1	Korkina LG, 2007	10.1170/T772	Phenylpropanoids as naturally occurring antioxidants: from plant defense to human health[24]	Cellular and Molecular Biology (1.5;Q4)	394	21.89
2	Salehi B, 2020	10.1021/acsomega.0c01818	Therapeutic Potential of Quercetin: New Insights and Perspectives for Human Health[25]	Acs Omega (3.7;Q2)	332	66.40
3	Gohil KJ, 2010	10.4103/0250-474X.78519	Pharmacological Review on Centella asiatica: A Potential Herbal Cure-all[26]	Indian journal of Pharmaceutical Sciences (0.5;Q4)	309	20.60
4	Suryakumar G, 2011	10.1016/j.jep.2011.09.024	Medicinal and therapeutic potential of Sea buckthorn (Hippophae rhamnoides L)[27]	Journal of Ethnopharmacology (4.8;Q1)	305	21.79
5	Panchatcharam M, 2006	10.1007/s11010-006-9170-2	Curcumin improves wound healing by modulating collagen and decreasing reactive oxygen species[28]	Molecular and Cellular Biochemistry (4.3; Q3)	304	16.00
6	Kumara B, 2007	10.1016/j.jep.2007.08.010	Ethnopharmacological approaches to wound healing–exploring medicinal plants of India[29]	Journal of Ethnopharmacology (5.4;Q1)	289	16.06
7	Arora R, 2005	10.1002/ptr.1605	Radioprotection by plant products: present status and future prospects[30]	Phytotherapy Research (7.2;Q1)	285	14.25
8	Neag MA, 2018	10.3389/fphar.2018.00557	Berberine: Botanical Occurrence, Traditional Uses, Extraction Methods, and Relevance in Cardiovascular, Metabolic, Hepatic, and Renal Disorders[31]	Frontiers in Pharmacology (4.4; Q1)	266	38.00
9	Salehi B, 2019	10.3390/molecules24071364	Piper Species: A Comprehensive Review on Their Phytochemistry, Biological Activities and Applications[32]	Molecules (4.2;Q2)	257	42.83
10	Saddiqe Z, 2010,	10.1016/j.jep.2010.07.034	A review of the antibacterial activity of Hypericum perforatum L[33]	Journal of Ethnopharmacology (5.4; Q1)	252	16.80

towards the modernization of conventional herbal resources for in-depth development. The evolution of the research, which focused from broad biological processes to specific organelles and molecular mechanisms, highlighted the growing understanding of the pathophysiology of cutaneous wound healing (Figure 4C and D). Advances in exploring specific molecular mechanisms and therapeutic approaches have led to research areas focusing on cellular senescence, matrix metalloproteinase-mediated angiogenesis for proliferative remodeling of granulation tissues, the pharmacological activity of herbal extracts, keratinocyte migration, extracellular matrix degradation, collagen deposition, novel drug carriers, and nanoparticle drug delivery.

Discussion

General Information Study

The study comprehensively analyzes the evolution, current landscape, and emerging trends in herbal medicine applications for wound healing over the past two decades. Since 2011, research has increasingly focused on natural products and their derivatives for clinical wound management, indicating a growing emphasis on this area of study. Additionally, research has expanded beyond the clinical efficacy of herbal extracts to encompass molecular-level mechanisms, including controlled drug delivery systems and the optimization of bioactive compounds.

Globally, China and Middle Eastern nations have driven research output, with Egypt leading in total publications. Indian institutions, particularly the CSIR, have historically been at the forefront of research in this field and have exerted a considerable degree of influence. Since 2007, Chinese institutions have experienced a rapid increase in publication volumes, propelling China to global leadership in output quantity. However, China's average citations per article lag behind those of the United States, indicating a need for enhanced international collaboration. Other countries, including Brazil, South Korea, Turkey, Italy, Mexico, Germany, Chile, and Australia, have also made valuable contributions to the development of this field, albeit to a lesser extent.

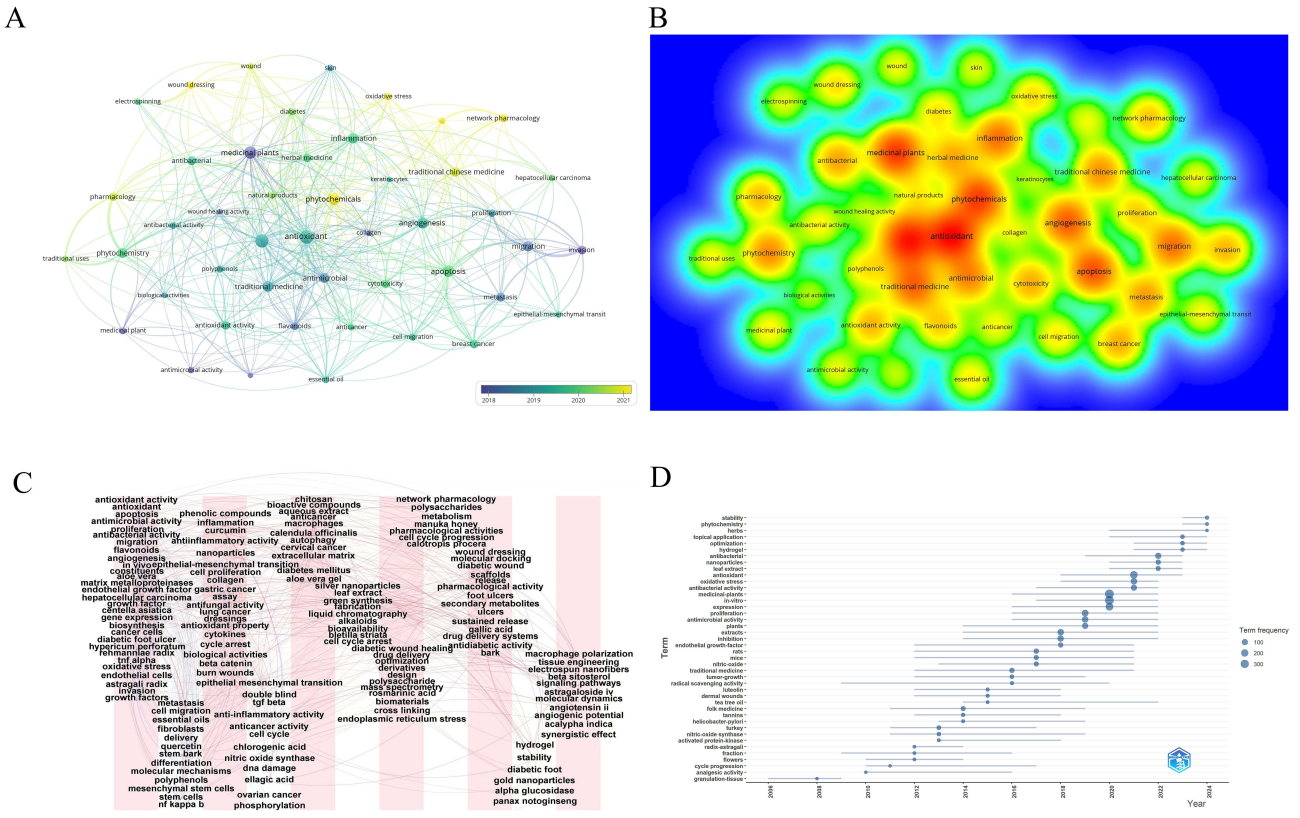

Figure 4 Visualization results of research hotspots: (**A**) Mapping time distribution of keywords in the research domain; (**B**) Keyword distribution according to the average frequency of occurrence; (**C**) Historiograph of articles; (**D**)Trend topics from 2001 to 2024.

The top 10 journals publishing this research span complementary and alternative medicine, botany, molecular biology, and pharmacology, reflecting its interdisciplinary nature. This diversity highlights both the field's vitality and the urgent need for translational research to bridge the gap between mechanistic discoveries and clinical applications. We encourage international collaboration among research institutions to promote innovation and address the multifaceted challenges associated with wound healing.

AKKOL EK and SUNTAR IPEK are the most relevant authors, indicating their significant impact on this research area. AKKOL EK has evaluated a wide range of medicinal plants and their secondary metabolites for their efficacy in wound healing, specializing in phytochemistry and pharmacology, particularly in analyzing the wound-healing potential of plants. He is also an expert in isolating and characterizing their active constituents by bioassay-guided methods.[34–51] SUNTAR IPEK[52] has assessed the wound healing and antioxidant activities of plant essential oils and their extracts, summarized the role of nuclear factor erythroid 2-related factor 2 (Nrf2) in the wound healing process, emphasized the importance of the Nrf2 signaling pathway in wound healing strategies, and highlighted its therapeutic potential in wound repair.[53]

The top 10 most cited articles focus on ethnopharmacology, oxidative stress, inflammatory response, and complementary and alternative medicine. The most cited study, "Phenylpropanoids as naturally occurring antioxidants: from plant defense to human health",[24] describes the synthetic and metabolic pathways and defense mechanisms mediated by phenylpropanoids in plants, as well as their anti-inflammatory and anti-tumor effects in vitro and in vivo through the modulation of molecular and cellular processes. These studies have shown that natural products such as quercetin, sea buckthorn, curcumin, berberine, piper, and hypericaceae exhibit multiple pharmacological effects, including antioxidant, anti-inflammatory, antimicrobial, and wound-healing properties, highlighting the powerful antimicrobial effects and primary health benefits of herbal products.[25,27,28,31–33] Arora [29] and Kumara [30] et al have reviewed and analyzed herbal plants used for free radical scavenging in Ayurveda, India's traditional system of medicine, and summarized a large

number of medicinal plants with wound healing activity and potential. These studies emphasize the active research surrounding the role of herbs and their products in wound healing. Future research may focus on accurately understanding the underlying mechanisms, identifying new therapeutic targets, and exploring potential clinical applications.

Hot Spots and Trends

Analysis of keyword frequency revealed substantial growth in wound healing research from 2014 to 2024, with notable emphasis on medicinal plants, antioxidant activity, and antimicrobial activity. This trend reflects the growing interest in wound healing research within the fields of medicine and pharmacology, as well as the gradual exploration of the potential of natural products and botanicals in wound healing. In recent years, research has increasingly focused on integrating modern biotechnology (eg, in vitro experiments) with traditional medicine (eg, medicinal plant extracts). The annual increase in mechanistic keywords reflects a transition from simple functional validation to an in-depth exploration of molecular mechanisms, including ischemia-reperfusion, collagen deposition, inflammatory mediator-induced programmed cell death, and chronic wound persistence caused by aberrant cell migration and proliferation. Early studies focused on broad biological processes such as oxidative stress and apoptosis, but have since narrowed to mechanisms and therapies at the micro-molecular level, particularly vascular neovascularization and re-epithelialization influenced by various signaling pathways. In recent years, the widespread application of modern technological tools has further advanced research into molecular mechanisms and the integration of multi-omics data. Emerging hotspots include nanoparticles, electrospun nanofibers, hydrogels, and metallic microneedles for drug delivery, reflecting a deeper understanding of wound healing therapy. Specific analyses and summaries are provided below.

As research on cell death and injury in wound healing progresses, programmed cell death (PCD) is thought to play a crucial role. Programmed cell death is an active and regulated form of cell death governed by genes, including apoptosis, autophagy, pyroptosis, necroptosis, ferroptosis, and cuproptosis.[54]

Apoptosis is considered a mode of programmed cell death associated with anti-inflammatory activity that modulates the immune response.[55] During wound healing, neutrophil apoptosis induces macrophage migration and phagocytosis, converting them from pro-inflammatory M1 macrophages to anti-inflammatory M2 macrophages, thus facilitating the transition of the wound from the inflammatory phase to the proliferative phase.[56] However, excessive apoptosis can induce overactivation of pro-inflammatory molecules, leading to persistent chronic inflammation and ultimately delayed wound healing. Herbal extracts have shown promising results in inhibiting apoptosis in wounds. However, most therapeutic studies remain in the preclinical stage, focusing on evaluating efficacy and exploring therapeutic mechanisms in experimental animal models. Several studies have shown that resveratrol can prevent endothelial cell apoptosis in a hyperglycemic environment. As a silent information regulator 1 (SIRT1) agonist, resveratrol stimulates c-Myc gene expression by accelerating the degradation of forkhead box O1 (FOXO1), thereby protecting endothelial cells (ECs).[57] Lei et al demonstrated that Panax notoginseng saponins inhibited the apoptosis of ECs, thereby promoting their proliferation and migration, leading to an effective improvement in diabetic wound healing.[58] Ginger extract activated the Akt/mTOR signaling pathway and increased the intracellular phosphatidylinositol 3-phosphate (PI3P) level, thus stimulating cell proliferation.[59,60] Ginsenoside Rg1 (Rg1) also upregulated SIRT1 expression to reduce apoptosis in ECs.[61] Fan et al reported that procyanidin B2 reduced apoptosis in endothelial progenitor cells (EPCs), a precursor cell of ECs, and alleviated oxidative stress to delay apoptosis.[62]

Current research continues to focus on apoptosis and autophagy, with a gradual shift toward pyroptosis and ferroptosis. In 2022, a new concept of cuproptosis was introduced.[63] Pyroptosis, a form of PCD induced by inflammation, is thought to shift cell fate towards apoptosis.[64] Necroptosis, typically activated when the apoptotic pathway is blocked, can trigger an inflammatory response similar to pyroptosis,[65] and is therefore considered an important factor in chronic wound pathogenesis. Lavender essential oil has been shown to accelerate lipopolysaccharide (LPS)-induced chronic wound healing by reducing the production of pro-inflammatory factors and alleviating the inflammatory response through the inhibition of macrophage pyroptosis.[66] Paeoniflorin inhibits NLRP3/ASC/caspase-1 inflammatory vesicle formation and NF-κB transcription by decreasing the chemokine receptor CXCR2, further inhibiting the release of pro-inflammatory cytokines, which reduces wound inflammation and accelerates healing.[67] Ferroptosis is a type of PCD that has been gradually recognized in recent years. It is mediated by iron-dependent lipid peroxidation characterized by

iron overload, reactive oxygen species (ROS) generation, and glutathione Peroxidase 4 (GPX4) inactivation.[68] Intracellular lipid peroxides are catalyzed by ferric ions to produce large amounts of reactive oxygen species, leading to the accumulation of inflammation, which in turn causes cell death.[69] Hesperidin (HST) has been shown to promote wound healing by inhibiting ferroptosis progression through activation of SIRT3.[70] Resveratrol can activate the Nrf2 pathway to inhibit ferroptosis induced by advanced glycation end-products (AGEs) in human umbilical vein endothelial cells (HUVECs), further promoting angiogenesis in diabetic wounds and accelerating wound healing.[71] Cuproptosis, a novel molecular event, was discovered and attracted attention in 2022. Similar to ferroptosis induced by iron accumulation, cytotoxicity occurs when the concentration of copper ions in the body becomes too high, leading to cell death.[63] There are fewer studies related to the mechanisms of pyroptosis, ferroptosis, and cuproptosis and their therapeutic agents, which can be deeply investigated in the future and will help to identify new therapeutic targets and promote clinical outcomes in wound healing.

Natural compounds exhibit great potential in the treatment of wound healing, particularly compounds such as polyphenols, tannins, flavonoids, and anthraquinones, which possess multiple biological activities. These compounds have anti-inflammatory, antibacterial, and antioxidant properties, promoting epithelialization and neovascularization, and mitigating scarring by modulating the immune response, scavenging reactive oxygen species, reducing apoptosis, and enhancing mitochondrial function. Curcumin effectively removes reactive oxygen species during the inflammatory phase and enhances granulation and collagen deposition in the proliferative remodeling phase.[72] Thymol and carvacrol stimulate the expression of vascular endothelial growth factor (VEGF) and transforming growth factor-β (TGF-β),[73,74] promote vascular regeneration, and facilitate epidermal crawling. Apigenin has been shown to upregulate mRNA expression of type-I and type-III collagen, activate the smad2/3 signaling pathway, and stimulate dermal collagen synthesis.[75] Asiaticoside significantly affects extracellular matrix (ECM) protein deposition, while the triterpenoid fraction markedly elevates fibronectin levels in human skin fibroblasts.[76,77] Astaxanthin (ASX), a carotenoid derived from oxygen-containing non-vitamin A sources, promotes skin wound healing in rats by suppressing inflammatory responses and fostering M2 macrophage polarization.[78]

Nanotechnology-based drug delivery systems are increasingly replacing conventional methods due to their enhanced bioavailability and target-specific precision. For instance, the encapsulation of quercetin, curcumin, and Danggui extract into liposomes incorporating heat-sensitive gels has been investigated, demonstrating enhanced penetration and prolonged drug release in a mouse model.[79–81] Nanohydrogels, characterized by their three-dimensional polymeric networks, maintained a moist wound environment while ensuring biocompatibility with epidermal tissues.[82] Nanohydrogels loaded with baicalin and cumquatoside were used in a mouse model of epidermal inflammation, where they proved effective in reducing inflammation and enhancing wound healing.[83,84] DPFI hydrogel promotes diabetic wound healing through rapid bactericidal action of polyethylenimine (PEI), slow-release scavenging of ROS by dihydromyricetin (DMY), and driving macrophage M1 to M2 polarization, pro-angiogenic/epithelial formation, and glucose regulation.[85] Berberine and chlorogenic acid (CGA) can self-assemble to synthesize supramolecular nanoparticles that exhibit better inhibition of Staphylococcus aureus and MRSA and promote wound healing.[86] Metal nanoparticles are widely used in clinical medicine due to their antibacterial, antimicrobial, and anti-inflammatory properties, attributed to their ability to bind to target cells, especially silver-based and gold-based nanostructures. Furthermore, nanoparticle integration with plant-derived bioactive compounds (eg, alkaloids, glycosides, essential oils) has shown superior therapeutic outcomes compared to traditional formulations.[87] Cell therapies such as mesenchymal stem cells (MSCs) and extracellular vesicles have shown promise in experimental chronic wound models. MSCs have been shown to block cellular pyroptosis and reduce the likelihood of ferroptosis.[88,89] However, the development of such novel technologies remains in its early stages. These approaches still face unique challenges related to biocompatibility, technical implementation, and clinical outcomes. With a deeper understanding of the mechanisms underlying these therapies and ongoing progress in related clinical studies, more effective treatments for chronic wounds are anticipated in the future.

Over the past decade, wound healing research has achieved substantial progress in understanding molecular mechanisms and therapeutic innovations. However, due to the complexity of its pathogenesis, the application of related theories to clinical practice has yet to achieve the expected outcomes. Based on the analysis of research hotspots, the following areas should be further emphasized in the future: 1. Systemic elucidation of natural product mechanisms

through multi-omics integration (genomics, metabolomics, proteomics) to decode bioactive compound interactions with wound microenvironments; 2. Accelerating the transition from preclinical studies to standardized clinical trials for herbal formulations, particularly focusing on dose optimization and safety validation; and 3. Cross-disciplinary integration, incorporating nanotechnology or biomaterials science, to develop intelligent wound repair systems. Therefore, researchers continue to face significant challenges and must further investigate the mechanisms underlying wound healing to develop more effective treatment strategies.

Limitations

This study presents a comprehensive historical analysis of the hotspots and scientific advances in the field of natural products in wound healing over the past two decades, utilizing bibliometric methods. The results of this study will contribute to a deeper understanding of the topic, thereby informing basic research and clinical treatments. Meanwhile, this study also has some limitations. First, this study is based solely on the WOSCC database, which may omit some non-English literature or emerging research results, potentially resulting in incomplete coverage of global research hotspots. Secondly, bibliometric analysis relies on specific technical tools and algorithms, which may lead to some degree of variation in the study results. Additionally, our study involved thorough data preprocessing and cleaning to minimize the impact of erroneous and duplicate data. However, this process may involve subjective judgments, such as identifying the literature to be examined and defining keywords, which may introduce subjectivity into the analysis results. Finally, although emerging directions such as nano-delivery systems have been proposed, their clinical translation still needs to be validated.

Conclusion

This study demonstrates the increasing recognition of the therapeutic potential of natural products in modulating pathological wound healing mechanisms. Through bibliometric and visualization analyses of 2394 publications from the WOSCC database, the study found that the number of publications in this field has been increasing annually. China is the most productive country, and the Egyptian Knowledge Bank stands as the most influential research organization in terms of output. AKKOL EK and LEUNG PC are the most influential authors. The JOURNAL OF ETHNOPHARMACOLOGY, MOLECULES, and PHYTOTHERAPY RESEARCH are the most influential journals. Research initially focused on keywords such as medicinal plants, oxidative stress, inflammation, antimicrobial activity, and apoptosis. In recent years, new hotspots, including pyroptosis, ferroptosis, collagen deposition, and nanodrug delivery, have emerged. In summary, Future research on natural products in wound healing should focus on multi-target synergistic mechanisms and translational applications. Interdisciplinary collaboration should be strengthened to explore the mechanism of natural product regulation on the microenvironment of chronic wounds, and to promote the translation of natural medicines from the laboratory to the clinic through rigorously designed clinical trials. This will help alleviate the healthcare burden associated with chronic wounds and improve patient outcomes.

Ethical Statements

Given that this was a bibliometric study without human participation, there was no need for ethical approval.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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