

A Bibliometric Analysis of *Aloe vera* in Wound Healing

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Received: 1 May 2023 ; Accepted: 29 May 2023; Published: 20 June 2023

Abstract

People have used *Aloe vera* for a variety of traditional medical applications. *A. vera* has been proven in numerous studies to play a key function in wound healing. Although there are many reviews on this topic, bibliometric analysis is not found in the literature. This study uses bibliometric analysis to evaluate the influence and relevance of the countries, journals, organizations, and authors that have made the most contributions to this topic. Scopus database was used to gather bibliographic data on relevant studies. A total of 417 published articles between 1981 and 2023 were selected. VOSviewer version 1.6.18 was used to conduct a bibliometric analysis of these papers. On the topic of *A. vera* as a wound healing agent, Tehran University of Medical Science from Iran was the most productive institution and Journal of Ethnopharmacology was the most productive journal. India was the most productive and collaborative country. The spotlight of the recent papers was the use of biotechnology techniques and drug-delivery strategies of *A. vera* in wound healing. Developing formulation using various drug-delivery methods followed by *in vivo* preclinical and clinical studies of this particular topic were potential to be explored.

Keywords: *Aloe vera*, wound healing, VOSviewer, bibliometric analysis, Scopus

INTRODUCTION

Nowadays, researchers have become interested in the use of natural products against disease and illness. Natural medicine typically has multiple broad complementary or synergistic effects on bodily systems (Karimi et al., 2015). *Aloe vera* is a kind of succulent plant and an evergreen enduring plant that originated in the Middle Eastern Promontory but now grows wild in tropical climates all over the world. It is well-known for its therapeutic benefits (Malik and Zarnigar, 2013). The colorless mucilaginous gel extracted from its leaves has been widely employed for pharmaceutical and cosmetic purposes (Sánchez et al., 2020).

The effects of *A. vera* in treating wounds have been studied, including the mechanism of action, preclinical trials, and clinical trials. Teplicki et al. (2018) investigated *A. vera*'s mechanism on wound healing. They found that *A. vera* promoted both fibroblasts' and keratinocytes' proliferation and migration. It also saved keratinocytes from preservative-induced mortality. In rats, it also raised

collagen levels and crosslinking in granulation tissue (Pandarinathan Chithra et al., 1998). *A. vera*-based extract of Nerium oleander demonstrated promise in healing skin burn injuries in animal models (Akgun et al., 2017). *A. vera* gel or ointment also reduced the REEDA scale on cesarean wound 24 hours after the operation (Molazem et al., 2014) and primiparous women's episiotomy wound (Eghdampour et al., 2013).

Researchers have found it difficult to track down relevant articles due to the recent significant expansion in the volume of study activity. Therefore, bibliometric analytic approaches were applied in managing this massive volume of data (Zupic and Čater, 2015). Most of the time, a bibliometric study is used to look at the number and quality of articles that have been published to find trends in a certain field of study (Zuraidi et al., 2022). The use of bibliometric software allowed for the investigation and analysis of a substantial amount of scientific data (Donthu et al., 2021). VOSviewer, the most frequently used bibliometric software, is used in the process of

constructing and displaying bibliometric correlations between a number of different variables. It helps researchers working in a particular subfield to do a search of publications and the citations that are associated with those papers (Kirby, 2023).

Bibliometric studies related to *A. vera* had been conducted. Fathima et al. (2022) gathered articles in *A. vera* from the Google Scholar database and conducted a bibliometric analysis of the top 100 cited articles. Bibliometric analysis of global research outputs of the genus *Aloe* and its biological activity from 2001 to 2020 was performed using VOSviewer (Adetunji et al., 2022). The articles were collected from two databases, Scopus and Web of Science. To the best of our knowledge, there has not been a bibliometric study performed on the effects that *A. vera* has on the healing of wounds. In this study, bibliometric analysis was used to examine articles on *A. vera* to help other researchers identify potential research topics, collaborators, and journals for publication of the therapeutic effects of *A. vera* on wounds.

RESEARCH METHODOLOGY

Data Collection and Extraction

The publications about *A. vera* in wound healing were collected from Scopus database in April 2023. The database provided by Scopus was chosen because it is more comprehensive and larger than Web of Science and it is useful for both keyword searches and citation analysis (Bamel et al., 2020; Effendi et al., 2021). The following search terms were used to collect data: (TITLE-ABS-KEY (“*Aloe vera*”) AND TITLE-ABS-KEY (“wound healing”)). The publications with the terms “*Aloe vera*” and “wound healing” in the title, abstract, or keywords were considered for the bibliometric analysis. No year restriction was applied.

Both automatic and manual filtering was used to improve the quality of collected data. Automatic filtering was used to eliminate the publications that were not written in English and were not original articles. To exclude

irrelevant publications, manual filtering was undertaken by reading the abstracts of the papers. Then, bibliographic data of selected papers were extracted into CRV format (file .crv) and exported using Visualization of Similarities viewer (VOSviewer) software as a bibliometric tool for subsequent analysis (Ha et al., 2020). The record-gathering and research paper elimination process is summarized in **Figure 1**.

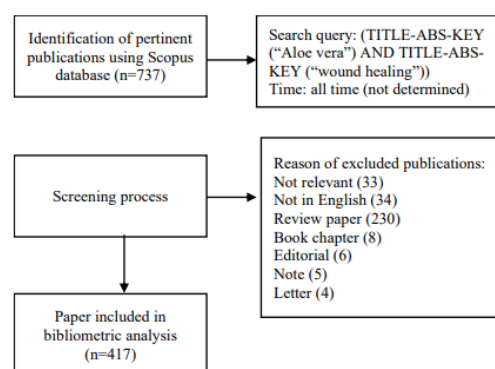


Figure 1. Paper selection and identification diagram

Data Analysis

The collected data was analyzed using VOSviewer software version 1.6.18. A trend analysis of publications by year was undertaken, illustrating the pattern of publications published on the topic of *A. vera*'s ability to treat wounds. The number of papers and citations were counted to assess the influence and impact of the research conducted. The co-occurrence analysis, co-authorship analysis, and citation analysis were performed using full-counting method and presented as network visualization maps. Using the full-counting method, the total weight of an analysis is equal to the number of links obtained as a result of the analysis (Perianes-Rodriguez et al., 2016). The terms (authors, keywords, and countries) are represented by a bubble. In the visualization, the size of the bubbles corresponds to the number of documents or occurrences of each term (Farhat et al., 2023; Yeung et al., 2020). The bubbles are linked together by

lines. The distance between two bubbles represents the relatedness of the co-authorship, co-occurrence, or bibliographic coupling between the terms (Romero and Portillo-Salido, 2019). The color of the bubble indicates the cluster to which the terms belong (van Eck and Waltman, 2022).

RESULT AND DISCUSSION

Publication Trends

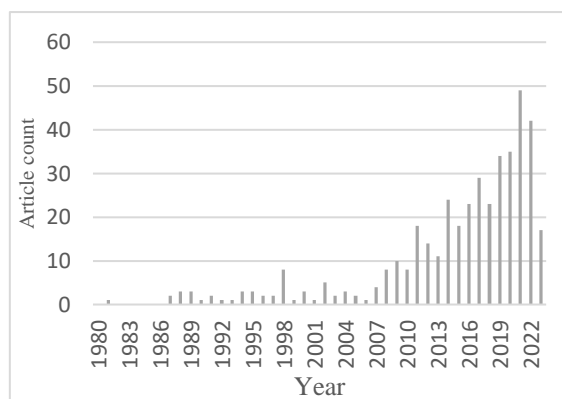


Figure 2. Publication trends on the topic of A. vera as a wound-healing agent

A total of 417 research articles about A. vera in wound healing were published between 1981 and 2023. The first paper

published by *Economic Botany* discovered that the fluid fraction of A. vera leaf extracts improved the healing of wounded cell monolayers (Winters et al., 1981). The latest paper published by *International Journal of Biological Macromolecules* developed thymol encapsulated in chitosan-A. vera films to prevent bacterial infection that contributed to delayed healing of wounds (Sharma et al., 2023).

The publication trends are shown in **Figure 2**. The number of publications on this topic has fluctuated throughout time. From 1981 to 2006, only two papers were published per year on average. Between 2007 and 2013, the annual publications grew slowly, with an average of 10 publications per year. More than 70.50 percent of the papers were published after 2013. Starting in 2014, the number of publications exceeded 20. The highest number of publications occurred in 2021 with 49 papers. Based on the observed publication trends, A. vera research in wound healing may continue to gain traction among researchers in the near future.

Table 1. Top 7 journals with the most papers

| No | Journal | Number of papers | Number of Citations | AC ¹ per paper | The title of the latest paper (year of publication) |
|----|--|------------------|---------------------|---------------------------|--|
| 1 | <i>Journal of Ethnopharmacology</i> | 18 | 1374 | 76.33 | Synergistic effect of Aloe vera flower and Aloe gel on cutaneous wound healing targeting MFAP4 and its associated signaling pathway: In-vitro study (2022) |
| 2 | <i>International Journal of Biological Macromolecules</i> | 16 | 856 | 53.50 | Thymol encapsulated chitosan-Aloe vera films for antimicrobial infection (2023) |
| 3 | <i>Journal of the American Podiatric Medical Association</i> | 7 | 555 | 79.28 | Aloe vera, hydrocortisone, and sterol influence on wound tensile strength and anti-inflammation (1994) |
| 4 | <i>International Journal of Pharmaceutics</i> | 5 | 220 | 44.00 | Aloe vera and copaiba oleoresin-loaded chitosan films for wound dressings: microbial permeation, cytotoxicity, and in vivo proof of concept (2023) |
| 5 | <i>Materials Science and Engineering C</i> | 5 | 211 | 42.20 | Investigations on the impact of the introduction of the Aloe vera into the hydrogel matrix on cytotoxic and hydrophilic properties of these systems considered as potential wound dressings (2021) |
| 6 | <i>Journal of Alternative and Complementary Medicine</i> | 5 | 164 | 32.80 | Thai herbal formulas used for wound treatment: A study of their antibacterial potency, anti-inflammatory, antioxidant, and cytotoxicity effects (2013) |
| 7 | <i>Carbohydrate Polymers</i> | 5 | 143 | 28.60 | Protein and polysaccharide-based asymmetric mat with tuned bilayer configuration for enhanced wound healing efficiency (2022) |

¹AC: average number of citations

Analyses of Contributing Journals

The 417 selected papers appeared in 281 different journals. The top 7 journals in terms of the number of papers on the use of *A. vera* for wound healing are shown in **Table 1**. They contributed 14.62 percent of the total number of corpus papers. The *Journal of Ethnopharmacology* comes out as the most productive journal of publication on this topic, with the most papers published (18) and the most citations (1374). The *International Journal of Biological Macromolecules* (16) and *Journal of the American Podiatric Medical Association* (7) are in second and third place, with 856 and 555 citations, respectively. The majority of these top 7 journals have published their most recent paper on this topic within the past five years. The aforementioned data will help academics find a specific journal and submit their research findings on this topic to those journals (Arifah et al., 2021). The *Journal of Ethnopharmacology* and *International Journal of Biological Macromolecules* could potentially be contacted to publish articles on the application of *A. vera* to wound healing.

Based on the top 7 journals' latest articles, studies on *A. vera* have progressed to the point where a drug delivery system is being formulated. The most recent articles from *Materials Science and Engineering C* revealed that *A. vera* juice enhanced hydrophilic characteristics in chitosan-based hydrogels. After 5 hours, the hydrogels were also able to release *A. vera* at the rate of 80% (Kudłacik-Kramarczyk et al., 2021). Genesi et al. (2023) developed 0.5% *A. vera*-loaded chitosan film. They confirmed that it was more effective than a commercial dressing film and the combination of chitosan and *A. vera* enhanced the wound-healing process. Sharma et al. (2023) developed thymol encapsulated in chitosan-*A. vera* and investigated its antimicrobial effect which contributed to wound-healing process. The outcome indicated that the developed product had potential antimicrobial activity.

Table 2. Top 10 countries with the most papers

| No. | Country | Number of papers | Number of Citations | AC ¹ per paper |
|-----|---------------|------------------|---------------------|---------------------------|
| 1 | India | 102 | 2690 | 26.37 |
| 2 | Iran | 70 | 1744 | 24.91 |
| 3 | United States | 45 | 1862 | 41.38 |
| 4 | Brazil | 25 | 650 | 26.00 |
| 5 | Indonesia | 20 | 100 | 5.00 |
| 6 | China | 18 | 398 | 22.11 |
| 7 | Pakistan | 16 | 449 | 28.06 |
| 8 | Thailand | 16 | 576 | 36.00 |
| 9 | Egypt | 15 | 331 | 22.07 |
| 10 | Saudi Arabia | 12 | 168 | 14.00 |

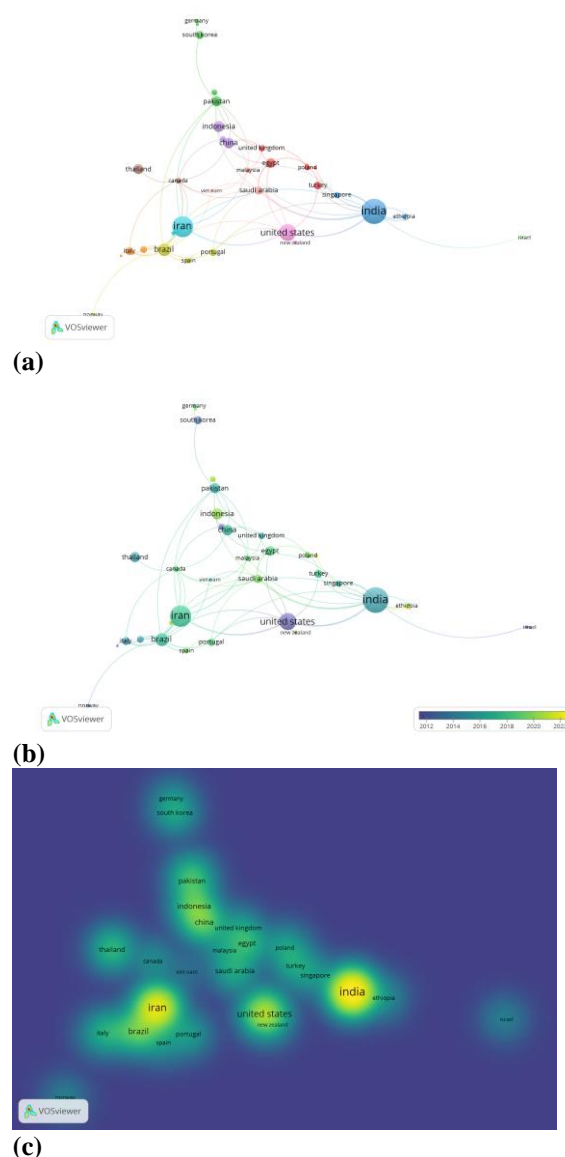


Figure 3. Network visualization (a), overlay visualization (b), and item density visualization (c) of contributing countries

Analyses of Contributing Countries and Their Collaborations

All selected papers came from 55 different countries. **Table 2** presents the top 10 countries that have published the most papers about using *A. vera* to heal wounds. The majority of the countries on the list were located in Asia. India provided the most papers (102), which accounted for more than 24.46 percent of the overall corpus. Iran (70), the United States (45), Brazil (25), and Indonesia (20) ranked second, third, fourth, and fifth, respectively, for the highest contribution in terms of paper count. The United States has a greater academic impact than the other countries based on average

citation per paper (41.38). From the average citation per paper perspective, Thailand (36.00) ranked second, followed by Pakistan (28.00), India (26.37), and Brazil (26.00).

The collaboration between countries was visualized using co-authorship analysis on VOSviewer. The network visualization map revealed twenty-three productive countries with at least one publication that collaborated with each other (**Figure 3a**). The size of the bubble is proportional to the number of publications produced by each country, and the thickness of the lines indicates the strength of collaboration between nation (van Eck and Waltman, 2022; Yu et al., 2020). India came in front with the largest bubble due to the

Table 3. Top 12 authors with the most papers

| No | Author name | Country | H-index | Number of Papers | Number of Citations | AC ¹ per paper | The title of the latest paper (year of publication) |
|----|-----------------------------|---------------|---------|------------------|---------------------|---------------------------|--|
| 1 | Davis, Robert H. | United States | 17 | 8 | 559 | 69.87 | Aloe vera, hydrocortisone, and sterol influence on wound tensile strength and anti-inflammation (1994) |
| 2 | Gupta, Amlam | India | 10 | 5 | 284 | 56.80 | Preparation and biological characterization of plasma functionalized poly(ethylene terephthalate) antimicrobial sutures (2020) |
| 3 | Ramakrishna, Seeram | Singapore | 159 | 5 | 249 | 49.80 | Biocompatible aloe vera and tetracycline hydrochloride loaded hybrid nanofibrous scaffolds for skin tissue engineering (2019) |
| 4 | Chandrakasan Gowri | India | 26 | 4 | 681 | 170.25 | Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats (1998) |
| 5 | Chithra, Pandarinathan | India | 10 | 4 | 681 | 170.25 | Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats (1998) |
| 6 | Sajithlal, Giangadharan B. | United States | 16 | 4 | 681 | 170.25 | Influence of Aloe vera on collagen turnover in healing of dermal wounds in rats (1998) |
| 7 | Gupta, Bhuvanesh D. | India | 41 | 4 | 233 | 58.25 | Preparation and biological characterization of plasma functionalized poly(ethylene terephthalate) antimicrobial sutures (2020) |
| 8 | Atiba, Ayman | Egypt | 7 | 4 | 169 | 42.25 | Topical and oral applications of Aloe vera improve healing of deep second-degree burns in rats via modulation of growth factors (2022) |
| 9 | Hegggers, John P. | United State | 51 | 4 | 248 | 62.00 | Retardation of wound healing by silver sulfadiazine is reversed by Aloe vera and nystatin (2003) |
| 10 | Hosseimehr, Seyed Jslal | Iran | 33 | 4 | 262 | 65.50 | The effects of Aloe vera cream on split-thickness skin graft donor site management: A randomized, blinded, placebo-controlled study (2011) |
| 11 | Oryan, Ahmad | Iran | 44 | 4 | 224 | 56.00 | Healing potential of injectable Aloe vera hydrogel loaded by adipose-derived stem cell in skin tissue-engineering in a rat burn wound model (2019) |
| 12 | Thunyakitpisa I, Pasutha D. | Thailand | 16 | 4 | 191 | 47.75 | Clinical and Radiographic Evaluation of Combined Acemannan and Periodontal Surgery Induced-Periodontal Regeneration: 5-Year Follow-up Case Report (2023) |

¹AC: average number of citations

paper's count and had the strongest collaboration with Saudi Arabia. India was also the top country with the most collaboration networks (11 countries). Brazil came in second place (10 countries), followed by the United States and Iran in third place, collaborating with nine countries. The overlay visualization (Figure 3b) shows that most of the countries' bubbles were colored green, blue, and purple. It indicated that the countries published their work in this field before 2020. The item density visualization (Figure 3c) shows that India and Iran have a strong yellow color intensity other than other countries, which indicates that they have a large number of publications on this topic.

Analyses of Contributing Authors and Their Collaborations

A total of 1795 authors contributed to the 417 papers. However, only 12 authors authored at least four papers. The number of research papers produced by an author reflects the author's contribution and engagement in this topic (Wu et al., 2021). The top 12 authors are listed in Table 3 based on the number of papers they have published on the selected topic. Numerous authors came from India. Davis R.H. ranks first with eight papers, ahead of Gupta A. and Ramakrishna S. each with 5 papers on *A. vera* as an agent for wound recovery. Based on average citation per paper, Chandrakasan G., Chithra P., and Sajithlal G.B. scored 170.25, followed by Davis R.H. (69.87). However, their last papers were published before 2000. Davis R.H., who came from the United States, published his last paper in 1994, which is quite a while ago. Among these top 12 authors, Thunyakitpisal P.D. from Thailand had the latest paper published in 2023.

To visualize the collaboration among the authors, co-authorship analysis was generated using VOSviewer. A minimum of one paper per author was set up. Among 1795 authors, only 64 authors constituted the largest set of linked authors in 10 clusters (Figure 4). The overlay visualization (Figure 4b) shows that

most of the authors published their work between 2015 and 2020. Most of the authors also had similar color density (Figure 4c) which indicated that overall authors produced a similar number of articles (Van Eck and Waltman, 2010). The total link strength was 208. Link strength reflects the number of papers co-authored by two authors (Lam et al., 2023). Ramakrishna S. had the highest link strength (19), indicating the most collaborative partners, followed by Kumar A.

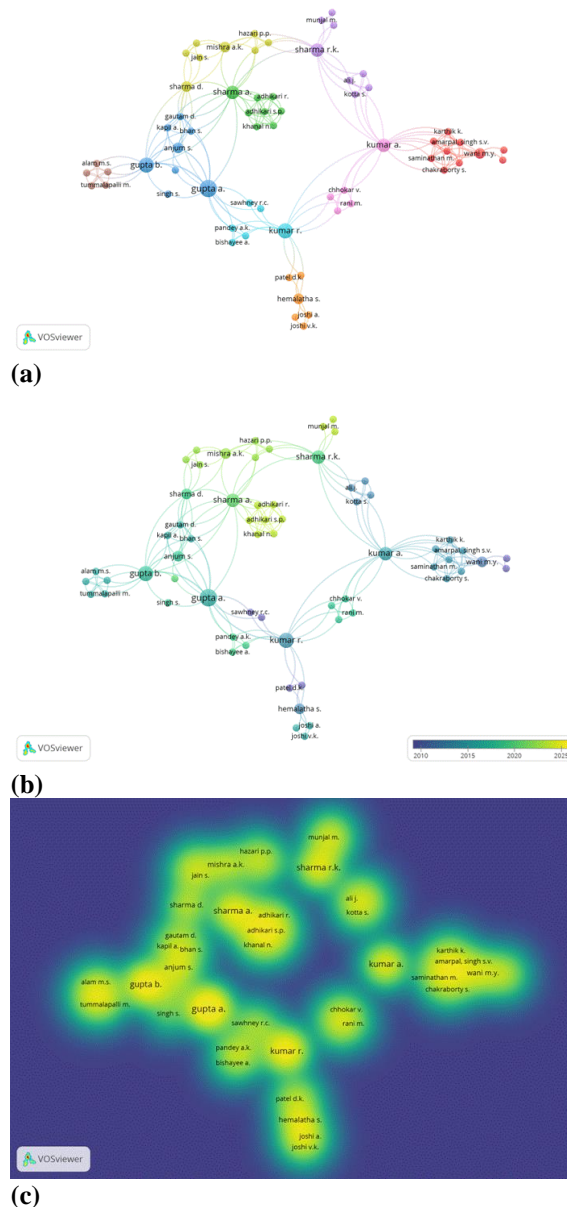


Figure 4. Network visualization (a), overlay visualization (b), and item density visualization (c) of contributing authors

Table 4. Top 6 institutions with the most papers

| No. | Institutions | Country | Number of Papers | Number of Citations | AC ¹ per paper | The title of the latest paper (year of publication) |
|-----|--|-----------|------------------|---------------------|---------------------------|---|
| 1 | Tehran University of Medical Science | Iran | 19 | 570 | 30.00 | Comparison of the effectiveness of Aloe vera gel with 2% nitrofurazone ointment on the healing of superficial partial-thickness burns: A randomized clinical trial study (2022) |
| 2 | Central Leather Research Institute India | India | 8 | 720 | 90.00 | Modular mucopolysaccharide gelatin naturapolyceutics hydrocolloid biomatrix with cobalt nano-additives for high density vascular network assembly (2021) |
| 3 | Anna University | India | 7 | 210 | 30.00 | Modular mucopolysaccharide gelatin naturapolyceutics hydrocolloid biomatrix with cobalt nano-additives for high density vascular network assembly (2021) |
| 4 | National University of Singapore | Singapore | 7 | 267 | 38.14 | Quercetin loaded silver nanoparticles in hydrogel matrices for diabetic wound healing (2021) |
| 5 | Chulalongkorn University | Thailand | 7 | 215 | 30.71 | Clinical and Radiographic Evaluation of Combined Acemannan and Periodontal Surgery Induced-Periodontal Regeneration: 5-Year Follow-up Case Report (2023) |
| 6 | Islamic Azad University | Iran | 7 | 181 | 25.86 | Evaluating the Effect of Supernatant Collected from the Culture of Bifidobacterium bifidum on the Increase of Angiogenesis in Acute Wound (2021) |

¹AC: average number of citations

(18) and Gupta A. (15). Ramakrishna S. published his latest papers on *A. vera* as a wound-healing agent in 2019 with title “Biocompatible Aloe vera and Tetracycline Hydrochloride Loaded Hybrid Nanofibrous Scaffolds for Skin Tissue Engineering”.

The most recent papers from the top 12 authors showed research in wound healing potential activity of *A. vera* had been done in various aspects. The influence of *A. vera* on wound tensile strength Field (Davis et al., 1994a) and the mechanism of its wound-healing activity Field (P. Chithra et al., 1998) were investigated before 2000. An advanced biotechnological approach was also applied to develop poly(ethylene terephthalate) sutures by plasma functionalization and immobilization of bioactive agent silver and *A. vera* (Anjum et al., 2020), *A. vera* hydrogel loaded by adipose stem cells (Oryan et al., 2019), and poly- ϵ -caprolactone, *A. vera*, and tetracycline hydrochloride hybrid nanofibrous scaffolds (Ezhilarasu et al., 2019). Clinical trials had been done to investigate the effect of *A. vera* cream on skin graft donor site wounds (Khorasani et al., 2011) and to look at how a

combination of acemannan (*A. vera* gel polysaccharide) and periodontal surgery affected periodontal regeneration (Chansamart et al., 2023).

Analyses of Contributing Institutions

One thousand one hundred eighty-eight institutions contributed to the 417 selected publications. Twenty institutions have influenced at least 5 publications, but only one had influenced more than 10. Tehran University of Medical Sciences from Iran produced the most publications (19) among the top seven institutions as measured by paper count (**Table 4**). Central Leather Research Institute India is ranked second with 8 papers, followed by Anna University, Nation University of Singapore, Chulalongkorn University, and Islamic Azad University, all of which have published seven papers. All of these institutions published recent papers in the last 2 years.

According to the number of citations, Central Leather Research Institute India ranked first with a number of citations of 720 and an average citation per paper of 90.00. It

indicates the papers produced by Central Leather Research Institute India are more influential than other institutions. For many years, citations have been used to evaluate the practicality of a research paper. Citation demonstrates the academic significance of a paper and how far to which it is recognized by other researchers (Mousavi-Jarahi et al., 2018).

According to the title of the most recent paper from the top seven institutions, clinical evaluation has been reached. In a randomized clinical trial study, *A. vera* gel promoted epithelialization and wound healing of partial-thickness superficial burns more effectively than 2% Nitrofurazone ointment (Varaei et al., 2020).

Keyword Co-occurrence Analysis

Table 2. Top 10 countries with the most papers

| No. | Keywords | Co-occurrences |
|-----|-----------------|----------------|
| 1 | Aloe vera | 164 |
| 2 | Wound healing | 118 |
| 3 | Chitosan | 22 |
| 4 | Wound dressing | 19 |
| 5 | Aloe vera gel | 19 |
| 6 | Wound | 14 |
| 7 | Aloe | 14 |
| 8 | Electrospinning | 13 |
| 9 | Hydrogel | 13 |
| 10 | Burn | 12 |

A keyword co-occurrence analysis was performed to find which terms commonly occurred in order to assist researchers in identifying the most popular subjects (Lin et al., 2022). Two words that occur frequently in a paper may have a closer relationship than other word pairings (Romero and Portillo-Salido, 2019). A total of 1055 keywords provided by the authors of the selected papers were analyzed. Only keywords that appear at least 5 times are visualized. Forty-two keywords were grouped into seven clusters, with 186 links and a total link strength of 448. The top 10 keywords from selected papers are presented in **Table 5**. “Aloe vera” appeared the most frequently, therefore it had the largest

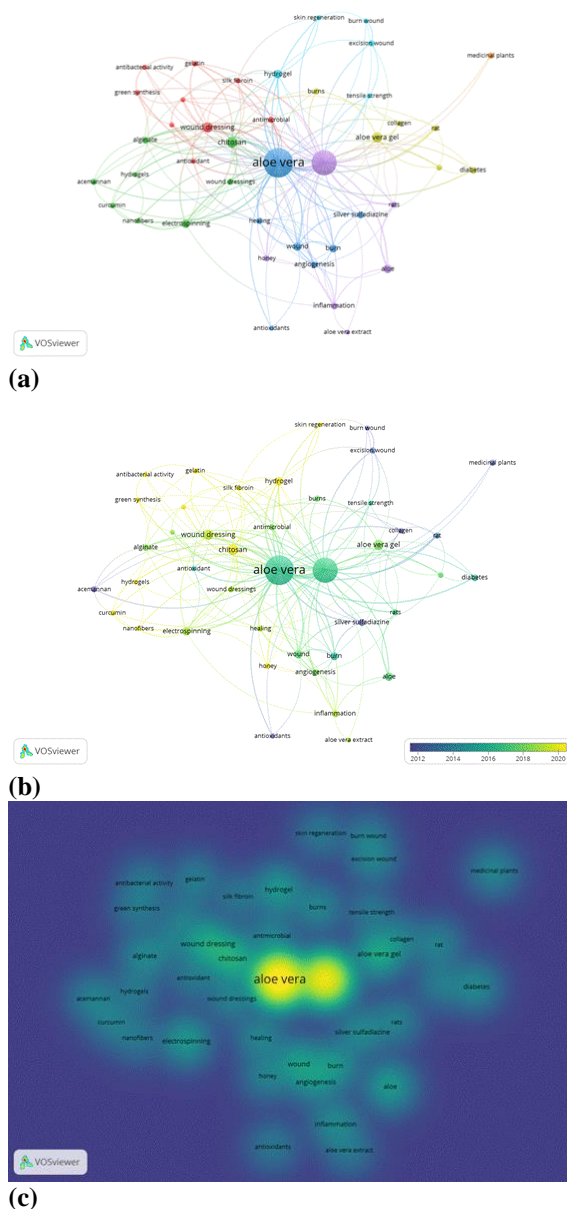


Figure 5. Network visualization (a), overlay visualization (b), and item density visualization of authors' keywords co-occurrence

bubble size (**Figure 5a**) and the strongest intensity of bubble yellow color (**Figure 5c**). It also had the most link, which was 38. It had a shorter distance with the bubble of “wound healing”, the second highest in terms of the number of occurrences, which indicated they had a larger number of co-occurrences (Yeung et al., 2022). The link line thickness directly reflects the terms' co-

Table 6. Top 10 most cited papers

| No. | Authors | Number of Citations | Title | Brief of studies |
|-----|---------------------------|---------------------|--|---|
| 1 | Pereira et al. (2013) | 270 | Development of novel alginate-based hydrogel films for wound healing applications | Aim: To evaluate the developed hydrogel film made up of alginate and <i>A. vera</i> gel in various proportions. Results: The developed hydrogel had sufficient mechanical characteristics for cutaneous applications and <i>A. vera</i> increased the transparency and thermal stability of the films. |
| 2 | Chithra et al., (1998) | 226 | Influence of Aloe vera on collagen turnover in healing dermal of wounds in rats | Aim: To evaluate the effect of <i>A. vera</i> on collagen turnover in full-thickness wounds on rats. Results: <i>A. vera</i> increased collagen turnover in the injured tissue. |
| 3 | Zhang and Tizard (1996) | 199 | Activation of a mouse macrophage cell line by acemannan: The major carbohydrate fraction from Aloe vera gel | Aim: To investigate the acemannan's effects on the murine macrophage cell line. Results: Acemannan has been shown to increase macrophage cytokine production, nitric oxide release, surface molecule expression, and the alteration of cell morphologic. |
| 4 | Chithra et al., (1998) | 196 | Influence of Aloe vera on collagen characteristics in healing dermal wounds in rats | Aim: To evaluate the effect of <i>A. vera</i> on collagen content and properties in wound healing in rats. Results: <i>A. vera</i> increased granulation tissue collagen content and crosslinking. |
| 5 | Yagi et al. (2002) | 192 | Antioxidant, free radical scavenging and anti-inflammatory effects of aloesin derivatives in Aloe vera | Aim: To investigate antioxidant components in <i>A. vera</i> . Results: Isorabaichromone (a derivate of aloesin) had significant antioxidative action and inhibitory effects on cyclooxygenase-2 and thromboxane A2 synthase. |
| 6 | Davis et al. (1994b) | 191 | Anti-inflammatory and wound healing activity of a growth substance in Aloe vera | Aim: To investigate anti-inflammatory and wound healing activity of Aloe vera in mice Results: Mannose-6-phosphate at 300 mg/kg enhanced wound healing in mice compared to saline controls. |
| 7 | Nordeng and Havnen (2004) | 190 | Use of herbal drugs in pregnancy: A survey among 400 Norwegian women | Aim: To investigate the use of herbal medicine in pregnant women by interviewing them. Results: During pregnancy, 36% of pregnant women had consumed herbal medicine with an average of 1.7 products per woman. |
| 8 | Choi et al. (2001) | 187 | The wound-healing effect of a glycoprotein fraction isolated from <i>A. vera</i> | Aim: To identify and isolate the components of <i>A. vera</i> that are responsible for wound healing. Results: <i>A. vera</i> 's wound-healing effect was mediated by its glycoprotein fraction. |
| 9 | Chithra et al. (1998) | 179 | The influence of <i>A. vera</i> on the glycosaminoglycans in the matrix of healing dermal wounds in rats | Aim: To investigate the effect of <i>A. vera</i> on the amount and types of glycosaminoglycans (GAGs) in the granulation tissue of healing lesions. Results: <i>A. vera</i> increased the synthesized of GAGs, in particular the types of hyaluronic acid, dermatan sulphate, and glycohydrolases. |
| 10 | Miguel et al. (2017) | 137 | Electrospun polycaprolactone/ Aloe vera_chitosan nanofibrous asymmetric membranes aimed for wound healing applications | Aim: To develop nanofibrous asymmetric membranes containing chitosan and <i>A. vera</i> for wound healing. Results: The developed membranes were comparable to native skin in porosity, wettability, and mechanical characteristics. |

occurrence strength (Feng and Chen, 2020). “Aloe vera” had the thickest link line with “wound healing”, “chitosan”, and “wound dressing”. It was also connected to “hydrogel”, “nanofibers”, “electrospinning”, “gelatin”, “alginate”, and “silver nanoparticles”, which were related to biotechnology, formulations, and drug delivery systems. It was also noticed that the author’s keywords were fairly varied, ranging from standard keywords such as “Aloe vera”, “wound healing”, and “medicinal plants” to nowadays advanced technology-used keywords such as “nanofibers”, “silk fibroin”, and “silver nanoparticles”.

The trend of keywords co-occurrence through time is presented in **Figure 5b**. All of the author’s keywords that appeared at least five times tended to start being used around 2012. Topics marked in blue bubbles were popular at the start of around 2012 and topics in green bubbles were more popular between 2014 and 2018. In the year after 2018, topics in yellow bubbles dominated.

The terms “excision wound”, “silver sulfadiazine”, and “medicinal medicine” tended to be the top 3 of the author’s keywords in the blue bubbles. Other keywords that appeared in the early years were “excision wound”, “burn wound”, and “wound healing activity”, which indicated research focused on conventional medical uses of *A. vera* in wound healing in this period. On the other hand, the top 3 of the author’s keywords in recent studies were “chitosan”, “hydrogel”, and “honey”. Other keywords that appeared in the current years were “green synthesis”, “silver nanoparticles”, and “nanofibers”. It showed that recent studies have focused on drug-delivery systems that use advanced biotechnological approaches.

According to this finding, drug-delivery strategies may have future research promise in terms of enhancing molecular bioavailability. Creating transdermal patches containing *A. vera* gel or extract for wound healing, for example, or creating a matrix containing *A. vera* for the manufacture of nanoparticles,

microparticles, or transdermal patches of chemical medicines to aid in wound healing could be ideas for future research. *In vivo* preclinical and clinical investigations can follow the drug-delivery strategy to elaborate on this specific issue.

Most Cited Papers

The top 10 most cited papers on the topic of wound healing effect of *A. vera* were listed in **Table 6**. Half of them came from published papers before the year 2000. The top 10 most cited papers received 137 to 270 citations, with an average of 201.3. The most cited papers by Pereira *et. al.* (2013) had a total of 270 citations. It also the most recent papers among the top 10. The research investigated the light transmission behavior, contact angle measurements, and chemical, thermal, and mechanical properties of the developed hydrogel film composed of alginate and *A. vera* gel. The results showed *A. vera* gel increased the transparency and thermal stability of the films. It also showed sufficient mechanical characteristics for use on the skin.

CONCLUSIONS

The current study revealed the advances in scientific understanding of *A. vera* and wound healing based on the publication retrieved from the Scopus database. We found a fluctuating number of papers from 1981 to 2023 on this topic. We also identified the most contributing journals (*Journal of Ethnopharmacology*), countries (India), and authors (Davis R.H.). Using keyword co-occurrence analysis and overlay visualization, we found the most popular keywords and their networks; and the current research hotspot. Keywords related to biotechnology approaches and drug-delivery strategies (such as “nanofibers”, “green synthesis”, “hydrogel”, “chitosan”, and “electrospinning”) dominated since 2018, indicating that the current research hotspot was developing new drug formulations by using these biotechnology approaches and drug-

delivery strategies. According to the title of the most recent studies from the most contributing countries and institutions, there were already clinical studies on the topic of *A. vera* in wound healing. We suggest that different drug-delivery techniques may have potential in future research, increasing the bioavailability of the molecule, followed by *in vivo* preclinical and clinical studies to expand this specific topic.

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