

Bibliometric Analysis of Herbal Used for Diabetic Foot Ulcer

Sekar Ayu Pratiwi¹, Triana Hertiani^{2*}

¹ Master in Pharmaceutical Sciences, Faculty of Pharmacy, Universitas Gadjah Mada

² Department of Pharmaceutical Biology, Faculty of Pharmacy, Universitas Gadjah Mada

Corresponding author: Triana Hertiani; Email: hertiani@ugm.ac.id

Submitted: 25-04-2024

Revised: 07-06-2024

Accepted: 07-06-2024

ABSTRACT

Diabetic Foot Ulcer (DFU) is a serious condition prevalent among diabetic patients. Due to its minimal side effects and cost-effectiveness, herbal remedies have garnered attention for DFU treatment. Many researchers are exploring effective herbal treatments. Bibliometric analysis serves as a tool to understand research focus and trends and identify extensively studied or underexplored herbs. In this study, publications related to herbal treatments for DFU were obtained from the Scopus database, where 90 articles meeting the inclusion criteria were analyzed using Vosviewer 1.6.20 software. The analysis was conducted using co-occurrence methods on titles and abstracts to provide an overview of herbal research for DFU, while co-occurrence methods on keywords offer a more detailed focus. Based on keyword analysis, the most frequently cited herb in the 90 articles over the past 10 years is Aloe Vera. Meanwhile, the analysis of titles and abstracts indicates that the most cited terms are "Angiogenesis," "Ointment," and "Infection." The findings of this study are expected to guide researchers in further exploring the potential of herbal treatments for DFU, thus contributing to the development of more effective and efficient therapies for diabetic patients suffering from foot ulcers.

Keywords: Bibliometric; Keyword Co-Occurrence; Diabetic Foot Ulcer (DFU); Herbal

INTRODUCTION

Diabetic Foot Ulcer (DFU) is a serious complication of diabetes. According to data from the Ministry of Health in 2021, Indonesia ranks among the top 10 countries with the highest number of diabetes patients. International Diabetes Federation (IDF) data from 2022 shows that there are 540 million people worldwide suffering from diabetes. In the Southeast Asian region, approximately 15% of diabetes patients experience DFU, with this number increasing annually. In patients with severe conditions, DFU can lead to amputation, increased morbidity rates, and decreased quality of life (Monteiro-Soares & Santos, 2022).

Interest in using herbal remedies to treat Diabetic Foot Ulcer (DFU) has significantly increased in recent decades. Herbs are known to have the potential to accelerate wound healing and reduce the risk of complications in this condition. Understanding the scientific publication trends related to the use of herbal remedies in treating DFU is crucial as it can provide valuable insights for researchers and medical practitioners in developing more effective treatment strategies. Through bibliometric studies, valuable information on research trends and recent developments in the use of herbal remedies for DFU treatment can be obtained (You et al., 2023). Bibliometric analysis using co-occurrence methods on keywords, abstracts, and article titles facilitates the identification of research trends and developments in the use of herbal remedies based on the frequency of occurrence of each term and their relationships with each other (Jiang et al., 2024; Wang et al., 2024).

METHODOLOGY

To ensure high-quality research data, in April 2024, journal selection was conducted on the internationally recognized Scopus database (www.scopus.com) using the keywords: (Herbal OR Extract AND Foot AND Ulcer and Diabetic). A total of 392 articles were found and screened based on the title and abstract, following the inclusion criteria of research articles published in the last 10 years (2015-2024), resulting in 90 articles. These articles were downloaded and their keyword information was analyzed using Mendeley. Subsequently, with the assistance of VOSviewer 1.6.20, data visualization was obtained based on keyword co-occurrence and text data analysis.

RESULT AND DISCUSSION

DFU is triggered by diabetic neuropathy and peripheral vascular disease, often accompanied by bacterial infections in the area, hindering the wound healing process. Additionally, factors such as age, blood sugar levels, nutritional management, and immune cell dysfunction play a role in influencing the wound-healing process in diabetic patients (Sanpinit et al., 2020). Research on DFU healing is generally focused on the wound closure process. Therefore, most identified herbs possess properties that support their role as wound closure agents. These properties include antioxidant, antibacterial, antimicrobial, antiseptic, and anti-inflammatory activities (Chokpaisarn et al., 2020).

Bibliometric analysis, especially through keyword analysis methods, provides an advantage to researchers by offering an in-depth understanding of the trends in herbal use for DFU treatment. By identifying evolving research patterns and primary focuses in scientific literature, this analysis can expedite the development of new drugs in the future (You et al., 2023).

Based on the analysis of 90 articles obtained, utilizing the co-occurrence keyword method in VOSviewer 269 keywords, further visualized in a diagram showing the relationships among keywords, as depicted in Figure 1. The analysis results formed 24 clusters, with each color representing a distinct cluster. The most frequently appearing keywords in the literature are "Diabetic Foot Ulcer" and "Wound Healing," as indicated by their large node sizes. From the network visualization, clustering based on similar colors among nodes can be observed. For instance, the keyword "Wound Healing" forms a cluster with keywords like "herbal turmeric," "areca catechu," "jinchuang ointment," and others.

To analyze the relationship between variables, the focus can be directed to each keyword, as illustrated in Figure 2a, where "Aloe Vera" is associated with the herbs "Plantain" and "Honey." In Figure 2b, "Angiogenesis" shows connections with the herbs "Rehmanniae Radix," "Ephedra Ciliata," and "Astragali Radix." Figure 2c demonstrates that the keyword "Biofilm" is linked with "Honey" and "Artemisia Vulgaris." Meanwhile, in Figure 2d, "Antibacterial" is connected to the herbs "Garcinia Mangostana" and "Areca Catechu."

In Figure 3, the overlay visualization reveals the patterns and trends in research development over the years. Recent research focuses on "Antiangiogenesis" and "Cell Proliferation." Additionally, two herbs recently studied about DFU are "Agave Applanata" and "Artemisia Vulgaris."

Table I presents the top 10 most researched herbs in the past decade. Aloe vera research dominates the literature keyword frequency, indicating its primary focus in diabetic foot ulcer treatment research. In patients with diabetes, the wound-healing process is impaired, and skin damage tends not to improve. Aloe vera has been proven to play a crucial role in enhancing cell proliferation and migration, stimulating vascular endothelial growth factor (VEGF) secretion, and preventing cell aging (Phimnuan et al., 2023). Furthermore, oral administration of aloe vera ethanol extract has been significantly shown to reduce blood glucose levels, increase plasma insulin levels, and glycosaminoglycans (GAGs) (Daburkar et al., 2014). To enhance efficacy, aloe vera is often used in combination with other herbs to achieve synergistic effects. In a study by Najafian et al. (2019), the combination of aloe vera and plantago major (plantavera) in gel form significantly reduced ulcer surface area (Najafian et al., 2018). Another study by Bahar et al. (2017) also showed that a combination of aloe vera gel and honey is effective in accelerating the wound healing process in diabetic foot ulcers (Bahar et al., 2015).

Additionally, Table II shows that the three most dominant traditional medicines related to DFU are from China. This indicates that traditional Chinese medicine plays a significant role in DFU treatment, which is interesting for further research to understand its potential and advantages.

Bibliometric analysis can also be conducted based on abstracts and titles in articles, where the frequency of each word in each title and abstract is visualized as shown in Figure 4. In this analysis, a minimum of 3-word co-occurrences has been selected, resulting in 245 terms subsequently analyzed, accounting for 60% of the total selected terms according to VOSviewer settings.

From the visualization results in Figure 4, 8 clusters are formed, each with its color-coded node. The three most frequently occurring words based on this visualization are "ointment," "angiogenesis," and "infection." It is important to note that visualization using abstracts and titles produces broader coverage of words compared to using keywords alone. This indicates that bibliometric analysis can help researchers find relationships among variables depending on their

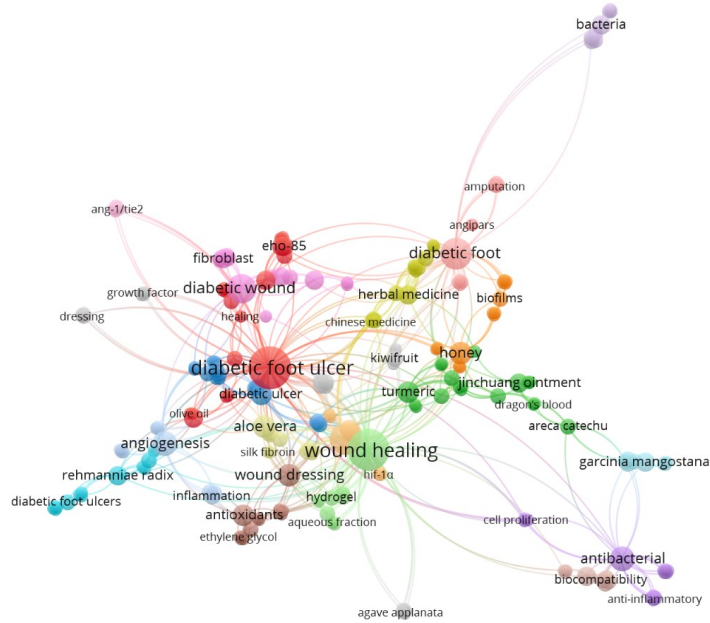
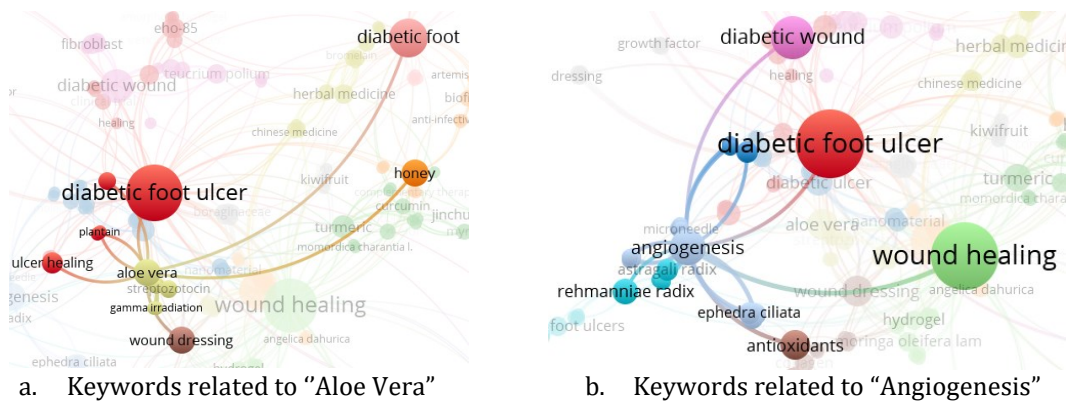


Figure 1. Network Visualization Keyword Analysis



a. Keywords related to "Aloe Vera"

b. Keywords related to "Angiogenesis"

c. Keywords related to "Biofilms"

d. Keywords related to "Antibacterial"

Figure 2. Interrelationship Among Variables

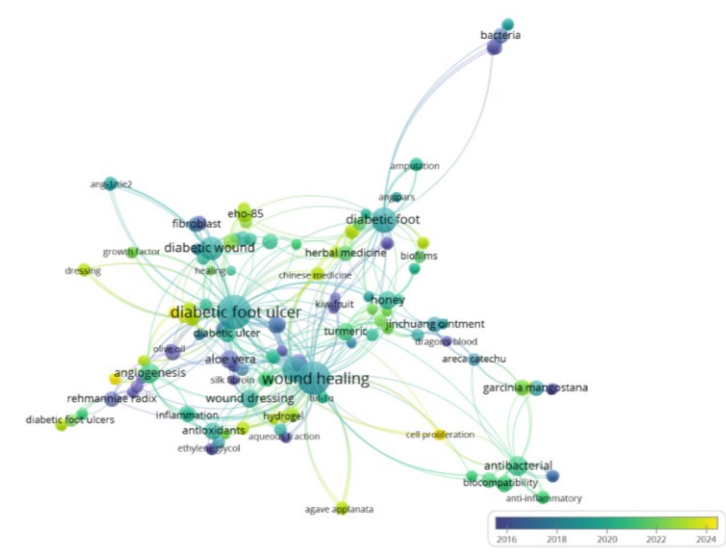


Figure 3. Overlay Visualization Keyword Analysis

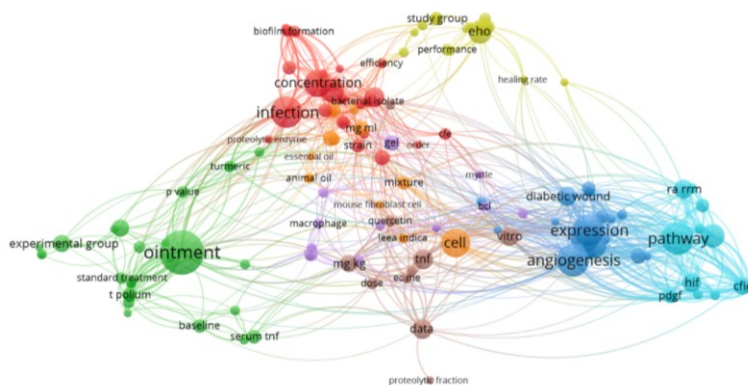


Figure 4. Network Visualization based on Title and Abstract

Table I. Top Ten Most Cited Herbs

No.	Keywords	Occurrences
1.	Aloe Vera	5
2.	Honey	5
3.	Turmeric	4
4.	Garcinia Magostana	3
5.	Rehmanniae Radix	3
6.	Ageratina Pichnchensis	3
7.	Asteraceae	3
8.	Olea Europaeae	3
9.	Moringa Oleifera Lam	2
10.	Plantago Major	2

Table II. Top Traditional Medicines

No.	Keywords	Occurrences
1.	Shenji Ointment	2
2.	EHO-85	3
3.	Jinchuang Ointment	3

individual needs. For a general overview, analysis based on titles and abstracts can be used, while for a deeper and more detailed understanding, keyword-based analysis is recommended.

CONCLUSION

Bibliometric analysis of DFU indicates significant progress and holds potential as a valuable knowledge source for future researchers. By leveraging data on herbal usage in DFU treatment obtained from bibliometric analysis, further research can enhance understanding of the effects and potential of extensively or minimally researched herbal remedies. The limited exploration of certain herbs, which may hold substantial potential in addressing DFU, underscores the need for subsequent researchers to delve into less focused variables, such as investigating side effects, optimal dosages, and mechanisms of action of underexplored herbs. Consequently, it is anticipated that this research could mitigate the risk of prolonged DFU effects, such as gangrene and amputation while improving healing rates and life expectancy for diabetic patients with foot ulcers.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENT

Thank you to all parties, especially the Master's Program in Pharmacy Sciences at Gadjah Mada University, for their assistance in the process of creating this article.

REFERENCE

- Bahar, A., Saeedi, M., Kshi, Z., Akha, O., Rabee, K., & Davoodi, M. (2015). The effect of Aleo vera and honey gel in healing diabetic foot ulcers. *Journal of Mazandaran University of Medical Sciences*, 25(128), 110–114.
- Chokpaisarn, J., Chusri, S., & Voravuthikunchai, S. P. (2020). Clinical randomized trial of topical Quercus infectoria ethanolic extract for the treatment of chronic diabetic ulcers. *Journal of Herbal Medicine*, 21(May 2018), 100301. <https://doi.org/10.1016/j.hermed.2019.100301>
- Daburkar, M., Lohar, V., Rathore, A. S., Bhutada, P., & Tangadpaliwar, S. (2014). An in vivo and in vitro investigation of the effect of Aloe vera gel ethanolic extract using animal model with diabetic foot ulcer. *Journal of Pharmacy and Bioallied Sciences*, 6(3), 205–212. <https://doi.org/10.4103/0975-7406.135248>
- Jiang, S., Pan, X., Li, H., & Su, Y. (2024). Global trends and developments in mindfulness interventions for diabetes: a bibliometric study. *Diabetology and Metabolic Syndrome*, 16(1), 1–18. <https://doi.org/10.1186/s13098-024-01288-x>
- Monteiro-Soares, M., & Santos, J. V. (2022). IDF Diabetes Atlas Report On Diabetes Foot-Related Complication. *International Diabetes Federation*.
- Najafian, Y., Khorasani, Z. M., Najafi, M. N., Hamed, S. S., Mahjour, M., & Feyzabadi, Z. (2018). Efficacy of Aloe vera/ Plantago Major Gel in Diabetic Foot Ulcer: A Randomized Double-Blind Clinical Trial. *Current Drug Discovery Technologies*, 16(2), 223–231. <https://doi.org/10.2174/1570163815666180115093007>
- Phimnuan, P., Dirand, Z., Tissot, M., Worasakwutiphong, S., Sittichokechaiwut, A., Grandmottet, F., Viyoch, J., & Viennet, C. (2023). Beneficial Effects of a Blended Fibroin/Aloe Gel Extract Film on the Biomolecular Mechanism(s) via the MAPK/ERK Pathway Relating to Diabetic Wound Healing. *ACS Omega*, 8(7), 6813–6824. <https://doi.org/10.1021/acsomega.2c07507>
- Sanpinit, S., Yincharoen, K., Jindamanee, C., Jobthin, S., Limsuwan, S., Kunworarath, N., Jaisamut, P., Chokpaisarn, J., Voravuthikunchai, S. P., & Chusri, S. (2020). Antibacterial properties of Ya-Samarn-Phlae (YaSP): A pilot study on diabetic patients with chronic ulcers. *Journal of Herbal Medicine*, 23(July), 100381. <https://doi.org/10.1016/j.hermed.2020.100381>
- Wang, Y., Wang, C., & Zheng, L. (2024). Bibliometric analysis of systematic review and meta-analysis on diabetic foot ulcer. *Heliyon*, 10(6), e27534. <https://doi.org/10.1016/j.heliyon.2024.e27534>
- You, J., Liu, C., Chen, Y., Zhu, W., Li, H., & Li, L. (2023). A Bibliometric Analysis of the Top-Cited Articles on Diabetic Foot Ulcers. *International Journal of Lower Extremity Wounds*, 22(3), 588–598. <https://doi.org/10.1177/15347346211034388>