Contents lists available atIOCS

Science Midwifery

journal homepage:www.midwifery.iocspublisher.org

Nanophytosome delivery system and in vivo test of combination of binahong leaf extract (Andredera cordifolia) and bay leaf (Syzygium polyanthum) as a diabetic wound healer

Arip Saifurrohman[1], Garnadi Jafar[2*], Entris Sutrisno[3], Fathurahman Ari Senjaya[4]
[1,2,3,4]Faculty of Pharmacy, Universitas Bhakti Kencana, Bandung, Indonesia

ARTICLEINFO

Article history:

Received Mar 4, 2026
Revised Apr 2, 2026
Accepted Apr 11, 2026

Keywords:

Bay Leaf
Binahong Leaf
Diabetic Foot Ulcer
In Vivo Study
Nanophytosome

ABSTRACT

This study aimed to develop and characterize a nanophytosome system containing combined extracts of bay leaf (Syzygium polyanthum) and binahong leaf (Anredera cordifolia), and to evaluate its wound healing activity through in vivo study. The extracts were prepared by maceration using 96% ethanol and characterized through phytochemical screening and LC-MS/MS analysis. Nanophytosomes were formulated using phospholipid complexes with variations of surfactants, followed by homogenization and sonication. The formulations were evaluated for particle size, polydispersity index, zeta potential, and entrapment efficiency. The results showed that particle size ranged from 16.30 to 927.18 nm, with the smallest size observed in Tween 80-based formulation. The polydispersity index ranged from 0.20 to 0.86, indicating better homogeneity in Tween 80 systems. Zeta potential values were in the range of −6 to −17 mV, suggesting moderate stability. Entrapment efficiency was high in all formulations (92.5–97.3%), with the highest value observed in Cremophor-based formulation. In vivo evaluation demonstrated that the nanophytosome significantly accelerated wound healing compared to control groups, as indicated by faster wound contraction and improved tissue regeneration. In conclusion, the nanophytosome system enhanced the physicochemical properties and delivery of bioactive compounds, showing potential as an effective therapeutic approach for wound healing.

Corresponding Author:

Garnadi Jafar,
Faculty of Pharmacy,
Universitas Bhakti Kencana,
Jl. Soekarno Hatta No. 754, Cipadung Kidul, Kec. Panyileukan, Kota Bandung, Jawa Barat, 40614, Indonesia
Email: garnadi.jafar@bku.ac.id

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia resulting from impaired insulin secretion, insulin action, or a combination of both. Persistent hyperglycemia can lead to damage in various organs, including the kidneys, nerves, blood vessels, and heart (H.

Sun et al., 2022). Globally, the prevalence of diabetes continues to rise and has become a major health concern with significant impacts on patients' quality of life(IDF, 2025).

One of the serious complications of diabetes mellitus is diabetic foot ulcer (DFU), a chronic wound in the lower extremities caused by peripheral neuropathy, vascular disorders, and infection. The wound healing process in this condition tends to be prolonged due to impaired tissue perfusion, increased oxidative stress, and a sustained inflammatory response (Armstrong et al., 2023). Therefore, therapeutic approaches are needed that not only reduce blood glucose levels but also accelerate wound healing.

The use of natural products as alternative therapies has gained increasing attention due to their bioactive compounds with potential antioxidant and anti-inflammatory properties. Bay leaves (Syzygium polyanthum) are known to contain major flavonoids such as quercetin, which exhibits strong antioxidant activity and plays a role in reducing oxidative stress and improving insulin sensitivity (Alwie et al., 2021). Quercetin has also been reported to accelerate wound healing through modulation of inflammatory responses and enhancement of cell proliferation (Firdaus et al., 2022).

Despite their significant therapeutic potential, the application of quercetin and kaempferol is still limited by major challenges such as poor solubility, limited stability, and low bioavailability. Therefore, an effective drug delivery system is required to enhance the stability and bioavailability of these compounds.

Nanotechnology in the pharmaceutical field has been developed as an advanced drug delivery approach, as nanoscale particles can increase surface area, enhance solubility, improve penetration ability, and protect active compounds from degradation (Jafar et al., 2022). One of the emerging approaches is the use of nanophytosome systems. Nanophytosomes are drug delivery systems based on complexes between phytochemical compounds and phospholipids, forming structures similar to cell membranes, thus improving compatibility with biological systems. Unlike conventional nanoparticles, nanophytosomes can directly bind to active compounds through hydrophobic interactions and hydrogen bonding, which enhances stability and protects the compounds from degradation(Kumar et al., 2020).

Furthermore, the nanoscale size of nanophytosomes offers advantages such as increased surface area and diffusion efficiency, which enhances penetration through biological membranes, including the skin. This system can also improve the permeability of active compounds by facilitating their transport through lipid bilayers, significantly increasing the bioavailability of compounds such as quercetin and kaempferol (Kumar et al., 2020).

Another advantage of nanophytosomes is their ability to provide controlled and sustained drug release, allowing drug concentrations to be maintained within the therapeutic range for a longer period. This is particularly important in the healing process of diabetic wounds, which requires continuous exposure to active compounds to overcome oxidative stress and chronic inflammation (Cheng et al., 2023). In addition, nanophytosome systems have been shown to enhance the chemical stability of flavonoid compounds against environmental factors such as pH, light, and oxidation, which are the main causes of active compound degradation (Yusuf et al., 2023).

RESEARCH METHOD

Instrument

The instruments used in this study included an analytical balance (Ohaus), a magnetic stirrer (IKA), a reflux apparatus set, a desiccator, a probe sonicator (Sonics Vibra Cell), and a particle size analyzer based on dynamic light scattering (Malvern Zetasizer) for measuring particle size, polydispersity index, and zeta potential. A Transmission Electron Microscope (TEM) (JEOL) was used to observe nanoparticle morphology. All instruments were calibrated prior to use to ensure accuracy and reliability of the measurements.

Material

The materials used in this study included thick extracts of bay leaves (Syzygium polyanthum) and binahong leaves (Anredera cordifolia) as active ingredients, phospholipids such as Phospholipon 90G, surfactants including Cremophor RH 40 and Tween 80, and 96% ethanol as the solvent. Additional materials for in vivo testing included rats, Sanoskin gel as a comparator, and alloxan monohydrate as a diabetes inducer. All materials were of pharmaceutical or pro-analysis grade and were obtained from reliable chemical suppliers.

Research Procedures

a. Preparation of Plant Raw Materials, binahong leaves were washed with running water and dried in an oven at 50°C for 72 hours. The dried samples were then ground into a homogeneous simplicia powder and stored in a closed container protected from light and moisture. Extraction was carried out using the maceration method with 96% ethanol at a ratio of 1:10 (w/v) for 3 days with occasional stirring. The filtrate was filtered using Whatman No. 1 filter paper and the process was repeated three times. The combined filtrates were then evaporated using a rotary evaporator to obtain a thick extract (Raaf et al., 2024).
b. Formulation of Nanophytosome Combination Extract, nanophytosomes of the combined binahong and bay leaf extracts were prepared using the reflux method. Initially, the thick binahong extract and surfactants were dissolved in 96% ethanol, while the phospholipids were dissolved in hot water. All solutions were mixed in a beaker and stirred until homogeneous. The mixture was then transferred into a round-bottom flask and refluxed at 50°C for 1 hour. Afterwards, the solution was placed in a desiccator for 1 hour to remove residual solvent. The mixture was then hydrated using a magnetic stirrer at 750 rpm and 50°C for 30 minutes. Finally, particle size reduction was performed using ultrasonication for 30 minutes until a clear and stable nanophytosome system was formed (Jafar et al., 2022).
c. Characterization of Nanophytosome Combination Extract, characterization of nanophytosomes included measurement of particle size, polydispersity index (PDI), zeta potential, entrapment efficiency (%EE), and particle morphology. Particle size and PDI were analyzed using a Malvern ZSP Zetasizer at 25°C after diluting the sample to 10 mL, where a particle size of <1000 nm indicates a good nanoparticle system and a PDI value <0.5 indicates a homogeneous size distribution. Zeta potential was measured using the same instrument with an electrode cuvette to evaluate system stability, where values greater than +30 mV or less than –30 mV indicate good stability. Entrapment efficiency (%EE) was determined using a centrifugation method at 12,000 rpm for 60 minutes, followed by analysis of free compounds in the supernatant using a UV–Vis spectrophotometer, calculated based on the ratio of total active compound to free active compound. Particle morphology was observed using TEM after sample dispersion, placement on a grid, staining with uranyl acetate, and drying prior to observation (Jafar et al., 2022).
d. In Vivo Test of Diabetic Wound Healing Activity in Mice, the experimental animals used were rats that had received ethical approval prior to the study. The rats were acclimatized for approximately 7 days at a temperature of around 24°C with ad libitum access to food and water, followed by initial body weight measurement (Anjani et al., 2021). The animals were divided into five groups: normal group (wound without induction and treatment), negative control (diabetic wound without treatment), positive control (diabetic wound treated with Sanoskin), and treatment groups receiving nanophytosome combination extract and crude combination extract. Diabetes was induced by intraperitoneal injection of alloxan until blood glucose levels exceeded 200 mg/dL. Subsequently, a linear incision wound (±3 cm depth) was made on the dorsal area using sterile instruments. The wound was cleaned with 70% ethanol and treated according to group allocation daily for 14–21 days. Wound healing was observed on days 1, 3, 5, 7, and 14 using a digital caliper (Panigrahi et al., 2025).

RESULTS AND DISCUSSIONS

Preparation of Plant Raw Materials

The extraction process of binahong leaf (Anredera cordifolia) and bay leaf (Syzygium polyanthum) simplicia was carried out using the maceration method with 96% ethanol as the solvent. After the extraction and concentration processes, yield calculations were performed to determine the efficiency of compound extraction from each material. The yield value was calculated based on the ratio of the obtained thick extract weight to the initial weight of the simplicia. The results of the extract yield calculation are presented in Table 1.

Table 1. Extraction yield of bay leaf and binahong leaf extracts

Extraction Method	Plant Material	Sample Weight (g)	Extract Weight (g)	Extraction Yield (%)
Maceration	Binahong leaf	500	72,2616	14.4
Maceration	Bay leaf	500	61.3750	12.27

Based on Table 1, the yield of binahong leaf extract (Anredera cordifolia) (14.4%) was higher than that of bay leaf (Syzygium polyanthum) (12.27%), indicating differences in extraction efficiency due to the characteristics of the raw materials. The higher yield in binahong is apparently associated with the presence of secondary metabolites that are more readily soluble in ethanol, such as flavonoids and polyphenols, as well as tissue structures that facilitate solvent penetration. These compounds are known to play a role in the wound healing process through their antioxidant, anti-inflammatory, and tissue regeneration-stimulating activities (Cedillo-Cortezano et al., 2024). Although the yield of bay leaf extract was lower, both extracts still have potential as sources of bioactive compounds, considering that extraction efficiency is also influenced by the nature of the material and the maceration conditions (Vitale et al., 2022).

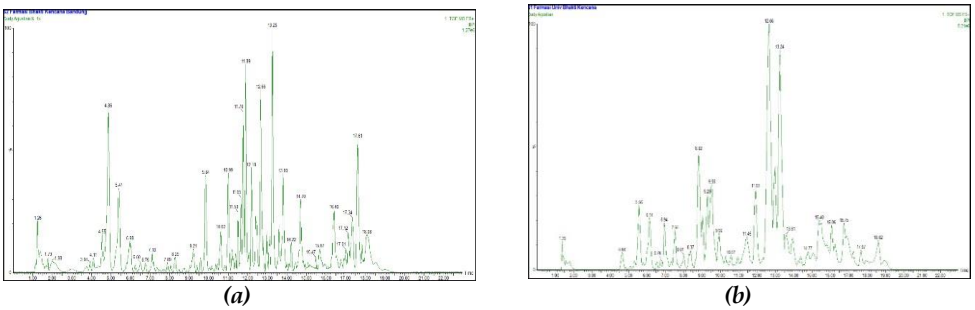
Table 2. Phytochemical screening of bay leaf and binahong leaf extracts

Phytochemical Compound	Test Method	Bay Leaf Result	BinahongLeaf Result
Alkaloids	Mayer	(+)	(+)
	Dragendorff	(+)	(+)
Flavonoids	Mg + HCl	(+)	(+)
Quinones	NaOH	(+)	(+)
Tannins	$FeCl_3$	(+)	(+)
	Gelatin	(+)	(+)
Saponins	Foam test	(+)	(+)
Steroids/Triterpenoids	Liebermann–Burchard	(-)	(-)

The phytochemical screening results (Table 2) showed that both extracts contained alkaloids, flavonoids, quinones, tannins, and saponins, while steroids/triterpenoids were not detected. The presence of these secondary metabolites indicates potential biological activities that contribute to the wound healing process. Flavonoids are known for their antioxidant activity, which can reduce oxidative stress and help regulate inflammation, thus accelerating the proliferation and epithelialization phases. In addition, tannins act as astringents that can promote wound contraction and new tissue formation, while saponins are known to stimulate collagen synthesis and angiogenesis (Cedillo-Cortezano et al., 2024).

LC-MS/MS (Liquid Chromatography–Tandem Mass Spectrometry) analysis was used to identify the metabolite profile of plant extracts qualitatively and semi-quantitatively. This technique combines compound separation based on retention time through liquid chromatography

with molecular mass detection using mass spectrometry, providing more specific information regarding the chemical composition of the sample. Through this method, the presence of various bioactive compounds in the extract can be detected with higher sensitivity and accuracy (Yan et al., 2022).



(a) *(b)*

Figure 1. LC-MS chromatograms of plant extracts: (a) bay leaf (syzygium polyanthum) and (b) binahong leaf (anredera cordifolia)

Based on the chromatograms in Figure 1, the extracts of bay leaf (Syzygium polyanthum) and binahong leaf (Anredera cordifolia) exhibited complex compound profiles, as indicated by the presence of multiple peaks at various retention times. The chromatogram of bay leaf (Figure 1a) showed a more widely distributed peak pattern with varying intensities, whereas binahong leaf (Figure 1b) displayed several dominant peaks with higher intensities, suggesting the presence of major compounds in greater quantities. This variation in profiles reflects differences in the composition of secondary metabolites in both extracts, which are known to contribute to biological activities, particularly as antioxidants and anti-inflammatory agents in the wound healing process through the regulation of oxidative stress and stimulation of tissue regeneration (Cedillo-Cortezano et al., 2024).

Formulations and Characterization of Nanophytosomes

In the formulation process, the reflux method is one of the commonly used techniques to form nanophytosome complexes. This method involves heating a mixture of active compounds and phospholipids at specific temperatures and durations to facilitate optimal molecular interactions. In this study, ten nanophytosome formulations were prepared with varying composition of phospholipids and surfactants to determine the most optimal formulation. Recent studies have shown that parameters such as reflux temperature, heating time, and phospholipid ratio significantly influence particle size, zeta potential, and entrapment efficiency of the resulting nanophytosomes (Chaerunisaa et al., 2025).

Table 3. Characterization of nanophytosome (particle size, PDI, zeta potential, and entrapment efficiency)

Code	NANOPHYTOSOME FORMULA					Z-Ave		ZP	%EE
	SON %	BAY %	PL %	TWE %	CRE %	nm	PdI	mV	%EE
NFTC F1	0.095	0.095	4	-	13.5	55.01±16.59	0.47±0.03	-17.03±2.79	97.3
NFTC F2	0.095	0.095	4.25	-	31.75	141.10±34.89	0.73±0.18	-6.49±3.13	94.7
NFTC F3	0.095	0.095	4.5	-	50	400.38±168.46	0.82±0.17	-9.47±2.51	94.2
NFTC F4	0.095	0.095	4.37	-	40.8	927.18±370.59	0.78±0.17	-14.26±1.92	94.8
NFTC F5	0.095	0.095	4.12	-	22.26	229.98±83.26	0.86±0.07	-13.50±1.86	95
NFTT F6	0.095	0.095	4	13.5	-	16.30±0.79	0.20±0.02	-11.48±4.62	97.2
NFTT F7	0.095	0.095	4.25	31.75	-	31.90±1.04	0.26±0.07	-15.29±0.82	94.1
NFTT F8	0.095	0.095	4.5	50	-	33.39±4.87	0.25±0.03	-14.29±1.38	94.8
NFTT F9	0.095	0.095	4.37	40.8	-	159.08±113.21	0.36±0.01	-13.89±2.11	95
NFTT F10	0.095	0.095	4.12	22.26	-	46.93 ± 0.43	0.39±0.15	-15.95±2.16	95.2

Information:

NFTC: Nanophytosome Chremophore®, NFTT: Nanophytosome Tween 80®, BIN: Binahong, PL: Phospolipon, TWE: Tween 80®, CRE: Chremophore®, PdI: Polydispersity Index, ZP: Zeta Potential

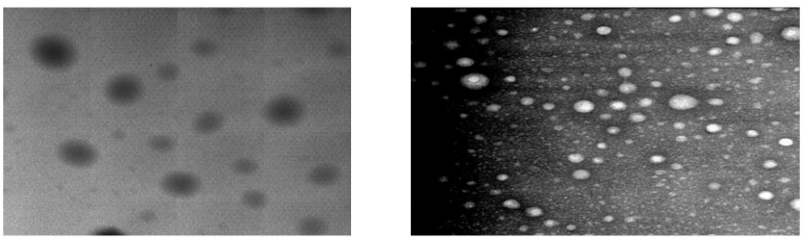
The characterization results in Table 3 indicate that variations in surfactant type and phospholipid concentration significantly affect particle size, polydispersity index (PDI), zeta potential, and entrapment efficiency (EE%) of the nanophytosomes. In formulations using Cremophor (NFTKC F1–F5), particle size increased from 55.01 nm (F1) to 927.18 nm (F4), which is likely due to particle aggregation at higher concentrations (Dwivedi et al., 2022). In contrast, the use of Tween 80 (NFTKT F6–F10) produced smaller particle sizes, with the smallest observed in F6 (16.30 nm), indicating better system stabilization (Khan et al., 2015).

The PDI values for Tween 80 formulations (0.20–0.26) indicate a more homogeneous particle size distribution compared to Cremophor formulations (up to 0.86). Meanwhile, the zeta potential of all formulations ranges from −6 to −17 mV, suggests moderate stability, which is still supported by the steric stabilization provided by non-ionic surfactants (Teli et al., 2024).

The EE% parameter showed that all formulations had high entrapment efficiency, ranging from 92.5% to 97.3%. The highest value was observed in NFTKC F1 (97.3%), while the lowest was found in NFTKT F8 (92.5%). The high EE% indicates that the nanophytosome system is capable of efficiently encapsulating active compounds through interactions between the polar groups of the compounds and phospholipids. Additionally, increasing phospholipid concentration tends to increase entrapment capacity, although under certain conditions it may also lead to increased particle size. This suggests a relationship between formulation composition and the encapsulation capability of the system (Dwivedi et al., 2025).

Overall, formulations using Tween 80, particularly NFTKT F6, demonstrated the most optimal characteristics based on small particle size and low PDI, while Cremophor-based formulations such as NFTKC F1 exhibited the highest EE%. Therefore, the selection of the optimal formulation should consider a balance between particle size, homogeneity, and entrapment efficiency.

Furthermore, particle morphology was evaluated using Transmission Electron Microscopy (TEM). The observations showed that the nanophytosome particles had a spherical shape with a relatively uniform size distribution. This spherical morphology is a common characteristic of vesicular systems such as phytosomes, formed through interactions between phospholipids and active compounds during the reflux process (Jafar, Putriyanti, et al., 2025). The resulting nanophytosome morphology indicates that the complex formation process occurred effectively, supporting system stability and enhancing the delivery efficiency of active compounds (Khan et al., 2015). The morphology of the nanophytosome particles is presented in Figure 2.



(a) **(b)**

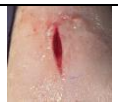
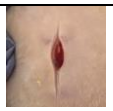
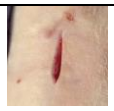
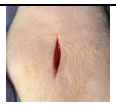
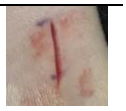
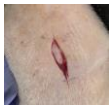
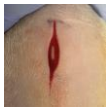
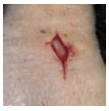
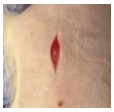
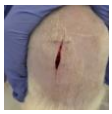
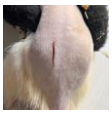
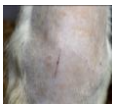
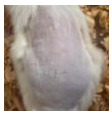
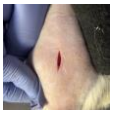
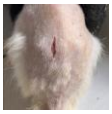
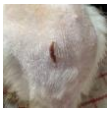
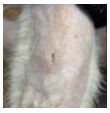
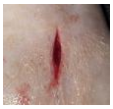
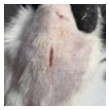
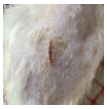
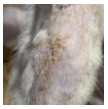
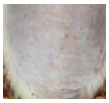
Figure 2. Morphology ofNanophytosomedroplets observed by Transmission Electron Microscopy (TEM): (a) blank nanoemulsion and (b) nanoemulsion containing combined extracts of bay leaf and binahong leaf

In Vivo Test of Diabetic Wound Healing Activity in Mice

Based on macroscopic observations of wounds in the in vivo Diabetic Foot Ulcer (DFU) model, significant differences in the speed and quality of wound healing between treatment

groups were observed during the observation period (day 1 to day 14). Observed parameters included wound contraction, granulation tissue formation, and the epithelialization process.

Table 4. Macroscopic observation of wound healing progression in diabetic foot ulcer (DFU) rat model across treatment groups

	T1	T3	T5	T7	T14
Group 1					
Group 2					
Group 3					
Group 4					
Group 5					

Information:
Group 1: Normal Control, Group 2: Negative Control, Group 3: Positive Control (Sanoskin Gel), Group 4: Nanophytosome Treatment, Group 5: Extract Treatment

In the normal group, wounds showed a progressive healing process, characterized by a narrowing of the wound size from day 3 (T3) and almost complete closure by day 14 (T14). This reflects the optimal progress of wound healing, which includes the hemostasis, inflammation, proliferation, and remodeling phases. This process involves complex interactions between fibroblasts, keratinocytes, and endothelial cells in the formation of new tissue and angiogenesis (Li et al., 2024).

In contrast, in the diabetes group without therapy, the wound healing process was slower, characterized by wounds that remained open until day 14. This condition is related to impaired wound healing in diabetes caused by chronic hyperglycemia, prolonged inflammation, and increased oxidative stress. Furthermore, dysfunctional angiogenesis and decreased cell proliferation also slow the re-epithelialization process and new tissue formation (Emad et al., 2024; Shi et al., 2024).

In the positive control group (Sanoskin), an increase in wound healing rate was observed compared to the untreated diabetic group. Wounds contracted more quickly and showed better tissue repair at the end of the observation period. This indicates that topical therapy can create an optimal wound environment, such as maintaining wound moisture and supporting cell migration, which are important factors in chronic wound healing (X. Sun et al., 2024).

In the nanophytosome (NFT) group, results showed a more significant acceleration in wound healing compared to the conventional extract group. Wounds contracted faster and showed better epithelialization on day 14. This effectiveness may be attributed to the use of a nanotechnology-based delivery system that can improve penetration, stability, and bioavailability of the active compound. The nanovesicle system is known to accelerate diabetic wound healing by increasing angiogenesis, reducing inflammation, and stimulating skin cell proliferation (Shi et al., 2024; X. Sun et al., 2024).

Additionally, lipid-based systems such as nanophytosomes have a high affinity for biological membranes, thereby enhancing the delivery of phytochemical compounds to target tissues. This contributes to increased collagen synthesis and accelerated re-epithelialization, which are important factors in wound tissue repair (Chettupalli et al., 2025).

Meanwhile, the binahong (Anredera cordifolia) and bay leaf (Syzygium polyanthum) extract groups showed better wound healing activity compared to the untreated diabetes group, although not as optimal as the nanophytosome group. This effect likely stems from the presence of bioactive compounds such as flavonoids and polyphenols, which have antioxidant and anti-inflammatory activity. These compounds are known to reduce oxidative stress, increase fibroblast proliferation, and accelerate granulation tissue formation (Emad et al., 2024; Nastiti et al., 2024).

Overall, the results of this study indicate that diabetes significantly inhibits the wound healing process. However, therapy, whether in the form of a positive control, herbal extract, or nanotechnology-based delivery system, can accelerate wound healing. Among all treatments, the nanophytosome system demonstrated the greatest potential, likely due to increased penetration and effectiveness of the active compounds in wound tissue.

CONCLUSION

A nanophytosome system containing a combination of bay leaf (Syzygium polyanthum) and binahong leaf (Anredera cordifolia) extracts was successfully formulated and has good characteristics such as particle size, PdI, Zeta Potential and % EE and has a spherical shape. In addition, the results of in vivo tests showed that nanophytosomes were able to accelerate the wound healing process compared to the control group. Thus, the nanophytosome system has the potential to be developed as an effective drug delivery system for natural-based wound healing therapy.

ACKNOWLEDGEMENTS

The author expresses his deepest gratitude to the Faculty of Pharmacy, Bhakti Kencana University, DKSH Indonesia, and RnD Bio Farma (Persero) for their invaluable support in providing research facilities and technical assistance, which contributed significantly to the smooth and successful conduct of this research. He also appreciates the constructive input and valuable suggestions from colleagues during the preparation of this manuscript.

References

Armstrong, DG, Tan, TW, Boulton, AJM, & Bus, S.A. (2023). Diabetic Foot Ulcers: A Review. In JAMA (Vol. 330, Number 1, pp. 62–75). American Medical Association. https://doi.org/10.1001/jama.2023.10578

Cedillo-Cortezano, M., Martinez-Cuevas, L.R., López, J.A.M., Barrera López, I.L., Escutia-Perez, S., & Petricevich, V.L. (2024). Use of Medicinal Plants in the Process of Wound Healing: A Literature Review. Pharmaceuticals, 17(3), 303. https://doi.org/10.3390/ph17030303

Cheng, X., Xie, Q., & Sun, Y. (2023). Advances in nanomaterial-based targeted drug delivery systems. Frontiers in Bioengineering and Biotechnology, 11. https://doi.org/10.3389/fbioe.2023.1177151

Chettupalli, A.K., Bukke, S.P.N., Vardhan, J., Yadhav, S., Mamilla Mugaiahgari, B.K., Jahnavi, P., Yata, V.K., & Narapureddy, B.R. (2025). Polyherbal formulations and phytosome-based delivery in diabetic wound healing: an integrative review. Journal of Biomaterials Science, Polymer Edition, 1–28. https://doi.org/10.1080/09205063.2025.2568684

Dwivedi, J., Wal, P., Kaushal, S., Tripathi, A.K., Gupta, P., & Prakash Rao, S. (2025). Phytosome based cosmeceuticals for enhancing percutaneous absorption and delivery. Journal of Research in Pharmacy, 29(1), 242–271. https://doi.org/10.12991/jrespharm.1643734

Emad, N.A., Zai, I., Ahmad, S., Pandit, J., Khan, M.A., & Sultana, Y. (2024). Role of Polyphenols, their Nano-formulations, and Biomaterials in Diabetic Wound Healing. Endocrine, Metabolic & Immune Disorders - Drug Targets, 24(6), 626–641. https://doi.org/10.2174/0118715303242310230927104709

Firdaus, M.N.A., Kardela, W., & Ifora, I. (2022). Phytochemical and Anti-Inflammatory Potential of Anredera cordifolia (Ten): A Review. Journal of Drug Delivery and Therapeutics, 12(2), 121–125. https://doi.org/10.22270/jddt.v12i2.5228

IDF. (2025). International Diabetes Federation - Diabetes Atlas 11th Edition.

Ilmiyah, SZ, Mamamia, A., Permana, S., Widodo, E., Norahmawati, E., Fakurazi, S., Malek, NANN, & Endharti, AT (2025). Recent advances and mechanism of action of Anredera cordifolia (Ten.) Steenis as anticancer approach: A systematic review. In Journal of Pharmacy and Pharmacognosy Research (Vol. 13, Number 2, pp. 369–380). Academic Association of Pharmaceutical Sciences from Antofagasta (ASOCIFA). https://doi.org/10.56499/jppres24.2044_13.2.369

Jafar, G., Salsabilla, S., & Santoso, R. (2022). DEVELOPMENT AND CHARACTERIZATION OF COMPRITOL ATO® BASE IN NANOSTRUCTURED LIPID CARRIERS FORMULATION WITH THE PROBE SONICATION METHOD. International Journal of Applied Pharmaceutics, 14(Special Issue 4), 64–66. https://doi.org/10.22159/ijap.2022.v14s4.PP04

Khan, S., Baboota, S., Ali, J., Khan, S., Narang, R., & Narang, J. (2015). Nanostructured lipid carriers: An emerging platform for improving oral bioavailability of lipophilic drugs. International Journal of Pharmaceutical Investigation, 5(4), 182. https://doi.org/10.4103/2230-973X.167661

Kumar, S., Baldi, A., & Sharma, D. K. (2020). Developing Drugs Phytosomes: A Modernistic Approach for Novel Herbal Drug Delivery-Enhancing Bioavailability and Revealing Endless Frontier of Phytopharmaceuticals. https://doi.org/10.4172/2329-6631

Li, Y., Zhu, Z., Li, S., Xie, X., Qin, L., Zhang, Q., Yang, Y., Wang, T., & Zhang, Y. (2024). Exosomes: process, biogenesis, and mechanisms in diabetic wound healing. Journal of Nanobiotechnology, 22(1), 398. https://doi.org/10.1186/s12951-024-02684-1

Nastiti, CMRR, Michelina, E., Wijayanti, FR, & Gani, MR (2024). Evaluation of Diabetic Wound Healing Activity of Novel Quercetin Topical Preparations. Journal of Pharmaceutical Sciences and Community, 21(1), 51–59. https://doi.org/10.24071/jpsc.007288

Panigrahi, L.L., Satpathy, S., Samal, P., Shekhar, S., Prusty, S.K., & Arakha, M. (2025). Biosynthesized iron oxide-nanoparticle encapsulated hydrogel functionalized with platelet-rich plasma (PRP) accelerates wound healing in an animal model. Nanoscale Advances, 7(22), 7209–7225. https://doi.org/10.1039/D5NA00621J

Prado-Gotor, R. (2022). New Avenues of Research for Nanoparticle Drug Delivery Systems. Nanomaterials, 12(23), 4141. https://doi.org/10.3390/nano12234141

Raaf, A., Mulana, F., Syamsuddin, Y., Suriaini, N., & Supardan, MD (2024). Effect of Drying Pretreatment Methods on Amla (Emblica officinalis) Extracts Obtained Through Maceration Using Ethanol as Solvent. International Journal of Technology, 15(4), 917. https://doi.org/10.14716/ijtech.v15i4.5669

Shi, S., Hu, L., Hu, D., Ou, X., & Huang, Y. (2024). Emerging Nanotherapeutic Approaches for Diabetic Wound Healing. International Journal of Nanomedicine, Volume 19, 8815–8830. https://doi.org/10.2147/IJN.S476006

Sun, H., Saeedi, P., Karuranga, S., Pinkepank, M., Ogurtsova, K., Duncan, BB, Stein, C., Basit, A., Chan, JCN, Mbanya, JC, Pavkov, ME, Ramachandaran, A., Wild, SH, James, S., Herman, WH, Zhang, P., Bommer, C., Kuo, S., Boyko, EJ, & Magliano, DJ (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Research and Clinical Practice, 183, 109119. https://doi.org/10.1016/j.diabres.2021.109119

Sun, X., Ding, H., Li, X., Wu, Y., & Huang, X. (2024). Disulfiram-loaded hydrogel nanovesicles promote healing of diabetic wounds. Journal of Translational Medicine, 22(1), 1066. https://doi.org/10.1186/s12967-024-05875-4

Teli, D., Satasia, R., Patel, V., Nair, R., Khatri, R., Gala, D., Balar, P.C., Patel, K., Sharma, A., Vadodariya, P., & Chavda, VP (2024). Nature meets technology: Harnessing nanotechnology to unleash the power of phytochemicals. Clinical Traditional Medicine and Pharmacology, 5(2), 200139. https://doi.org/10.1016/j.ctmp.2024.200139

Vitale, S., Colanero, S., Placidi, M., Di Emidio, G., Tatone, C., Amicarelli, F., & D'Alessandro, A. M. (2022). Phytochemistry and Biological Activity of Medicinal Plants in Wound Healing: An Overview of Current Research. Molecules, 27(11), 3566. https://doi.org/10.3390/molecules27113566

Yan, S., Bhawal, R., Yin, Z., Thannhauser, T. W., & Zhang, S. (2022). Recent advances in proteomics and metabolomics in plants. Molecular Horticulture, 2(1), 17. https://doi.org/10.1186/s43897-022-00038-9

Yohana Chaerunisaa, A., Muhaimin, M., Nur Fatimah, S., Kusuma Dewi, M., Amalia, R., & Fauziyah Sutisna, S. (2025). Cytotoxic Activity of Ethanolic Extract of Zanthoxylum acanthopodium DC. Fruit as

Phytosomal System against MCF-7 Cell Line. Trends in Sciences, 22(11), 10536. https://doi.org/10.48048/tis.2025.10536

Yusuf, A., Almotairy, ARZ, Henidi, H., Alshehri, OY, & Aldughaim, MS (2023). Nanoparticles as Drug Delivery Systems: A Review of the Implications of Nanoparticles' Physicochemical Properties on Responses in Biological Systems. Polymers, 15(7), 1596. https://doi.org/10.3390/polym15071596