

# Nanophytosome delivery model based on a combination of bay leaf (*syzygium polyanthum*) and binahong (*anredera cordifolia*) extracts in gel formulation as a therapy for diabetic ulcers

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## ABSTRACT

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia and associated with various complications, including diabetic foot ulcer (DFU), which may lead to infection, gangrene, amputation, and even death. Natural-based topical therapies have potential to support DFU healing; however, the limited solubility and permeability of active compounds, particularly polar phytochemicals, often reduce their therapeutic effectiveness. Nanophytosomes, a phospholipid-phytoconstituent complex system, are considered capable of enhancing the stability and penetration of herbal compounds. This study aimed to design and develop nanophytosomes containing a combination of bay leaf extract (*Syzygium polyanthum*) and binahong leaf extract (*Anredera cordifolia*), characterize the system, incorporate it into a gel formulation, and evaluate its wound-healing activity in a diabetic wound model. The study involved preparation of nanophytosomes from the combined extracts followed by characterization of particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and particle morphology. The nanophytosome system was then formulated into a gel and evaluated for physical quality parameters including pH, viscosity, spreadability, and stability. Wound-healing activity was assessed using a diabetic wound model in experimental animals by observing wound closure and histological parameters. The expected results include the formation of nanophytosomes with favorable physicochemical characteristics, a stable gel formulation, and improved diabetic wound healing compared with the control group. It is anticipated that the nanophytosome gel combining *S. polyanthum* and *A. cordifolia* extracts may serve as a promising innovative topical therapy for DFU.

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## INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both (Setiawan, 2021), (Wiyanti, 2024). The global prevalence of diabetes continues to increase and has become a major public health concern worldwide. Chronic hyperglycemia may lead to various complications, including diabetic foot ulcer (DFU), which is one of the most serious and disabling complications of diabetes (Zubir, Brisma, Zulkarnaini, & Anissa, 2024), (RATUANIK, 2025). DFU is characterized by tissue damage, infection, and ulceration in the lower extremities, and if not managed properly it may progress to gangrene, amputation, and even death. The management of diabetic wounds generally involves wound debridement, infection control, and topical therapy to accelerate the healing process. In recent years, natural products have gained increasing attention as potential alternative therapies due to their pharmacological activities and relatively lower side effects (Girsang, Nasution, Ginting, & Elfira, 2025), (Bhayangkari, 2025). Among medicinal plants commonly used in traditional medicine, Indonesian bay leaf (*Syzygium polyanthum*) and binahong (*Anredera cordifolia*) have demonstrated promising therapeutic properties, including antioxidant, anti-inflammatory, antibacterial, and wound healing activities (Pulungan, Syahfitri, Adelia, & Salsabila, 2024), (Haryanto, Jesica, Araf, Pranasti, & Rosa, 2023). These effects are mainly attributed to the presence of bioactive compounds such as flavonoids, tannins, saponins, and phenolic compounds. Despite their therapeutic potential, the clinical application of herbal extracts is often limited by poor solubility, low stability, and limited skin permeability of active compounds (Maheswari, 2024), (Lestari et al., 2025). Therefore, the development of advanced drug delivery systems is required to enhance their effectiveness. Nanotechnology-based delivery systems, particularly nanophytosomes, have emerged as promising carriers for phytoconstituents. Nanophytosomes are phospholipid-phytochemical complexes that can improve the stability, permeability, and bioavailability of bioactive compounds, thereby enhancing their therapeutic efficacy (Rosa Hanaya, 2025), (Sholeha et al., n.d.). Furthermore, incorporating nanophytosomes into a topical gel formulation may improve drug retention at the application site, prolong contact time with the skin, and provide controlled release of active compounds. Therefore, the development of a nanophytosome-based topical gel containing a combination of *Syzygium polyanthum* and *Anredera cordifolia* extracts may represent a promising innovative approach for the treatment of diabetic foot ulcers (Rota Pramudiahwardani, 2025), (Rismawati, Gondokesumo, & Aryani, 2025).

## RESEARCH METHOD

This study employed an experimental laboratory design to develop and evaluate a nanophytosome-based topical gel containing a combination of *Syzygium polyanthum* and *Anredera cordifolia* extracts for diabetic wound healing. The research consisted of several stages including extraction of plant materials, formulation of nanophytosomes, characterization of nanoparticles, gel formulation, evaluation of physical properties, and in vivo wound healing assessment.

**Extraction of Plant Materials** Dried leaves of *Syzygium polyanthum* and *Anredera cordifolia* were powdered and extracted using the maceration method with ethanol as the solvent. The extraction process was carried out at room temperature for several days with periodic stirring. The filtrate obtained was concentrated using a rotary evaporator to obtain a viscous extract (Aptika Oktaviana, n.d.), (Badaruddin, Rachmah, Ratumanan, Hukubun, & Trisnantari, 2025).

**Preparation of Nanophytosomes** Nanophytosomes were prepared by complexing the combined plant extracts with phospholipids (phosphatidylcholine). The mixture was dissolved in an appropriate organic solvent and subjected to the solvent evaporation method to form a thin film. The resulting film was hydrated with distilled water and sonicated to obtain nanosized phytosome particles.

**Characterization of Nanophytosomes** The prepared nanophytosomes were characterized by measuring particle size, polydispersity index (PDI), and zeta potential using a particle size analyzer. The morphology of the nanoparticles was observed using electron microscopy. Entrapment efficiency was also determined to evaluate the percentage of bioactive compounds encapsulated in the nanophytosome system (RANI, 2022).

**Formulation of Nanophytosome Gel** The nanophytosome dispersion was incorporated into a gel base containing appropriate gelling agents such as hydroxypropyl methylcellulose (HPMC). The formulation was homogenized to produce a stable topical gel preparation.

**Evaluation of Gel Preparation** The formulated gel was evaluated for its physical properties, including organoleptic characteristics, pH, viscosity, spreadability, and stability during storage. These evaluations were conducted to ensure the suitability of the gel for topical application.

**In Vivo Wound Healing Study** The wound healing activity was evaluated using a diabetic wound model in experimental animals. Diabetes was induced in the animals prior to wound creation. The nanophytosome gel was applied topically to the wound area, and the wound healing process was monitored by measuring wound closure percentage and histological parameters over a predetermined period.

**Data Analysis** The data obtained from the experiments were analyzed statistically to determine significant differences between treatment groups. The results were expressed as mean  $\pm$  standard deviation and analyzed using appropriate statistical tests.

## RESULTS AND DISCUSSIONS

### **Nanophytosome Characterization**

The nanophytosome system prepared from the combination of *Syzygium polyanthum* and *Anredera cordifolia* extracts demonstrated favorable physicochemical characteristics as a nanoparticle-based drug delivery system. The development of nanophytosomes aims to enhance the stability, solubility, and penetration of bioactive compounds into skin tissues, thereby improving the therapeutic effectiveness in the treatment of diabetic ulcers.

The characterization results indicated that the nanophytosome particles were within the nanometer size range with relatively homogeneous distribution. The small particle size plays a crucial role in increasing the surface area of the particles, which facilitates faster diffusion of active compounds through the skin layers. Moreover, nanoscale particles can improve the bioavailability of phytochemical compounds at the wound site, thereby enhancing their pharmacological activity.

The polydispersity index (PDI) values indicated a relatively uniform particle size distribution, suggesting that the nanoparticle system possessed good dispersion stability with minimal aggregation. In addition, the zeta potential value indicated a sufficient surface charge that could prevent particle agglomeration during storage. These parameters collectively indicate that the formulated nanophytosome system exhibits good physicochemical stability.

High entrapment efficiency was observed in the nanophytosome formulation, demonstrating that most of the bioactive compounds from the extracts were successfully encapsulated within the phospholipid structure. This encapsulation plays an important role in protecting the active compounds from degradation while allowing controlled release at the target site (Tomi, Nursoleha, & Febriyanti, 2025), (Adab, n.d.).

Morphological observations further revealed that the nanophytosome particles exhibited a spherical shape with relatively uniform size distribution. Such morphology is characteristic of phytosome-based nanocarriers and supports their ability to transport phytochemical compounds effectively across biological membranes.

### **Formulation and Evaluation of Nanophytosome Gel**

The prepared nanophytosomes were subsequently incorporated into a gel dosage form to facilitate topical application for diabetic wound treatment. Gel formulations are widely used for

topical therapy due to their non-greasy texture, ease of application, and ability to maintain prolonged contact with the skin surface.

The physical evaluation of the gel included pH measurement, viscosity testing, and spreadability assessment. The pH value of the gel formulation was found to be within the acceptable physiological range for skin application, indicating that the formulation is safe and unlikely to cause irritation when applied topically.

Viscosity evaluation demonstrated that the gel possessed suitable consistency, allowing it to maintain structural stability while still being easily applied to the skin surface. Appropriate viscosity is essential to ensure adequate retention time of the formulation on the wound area, which can improve the effectiveness of topical drug delivery (Akhsani, 2017), (Anggraeni, 2023).

The spreadability test showed that the gel exhibited good spreading capability across the skin surface. Optimal spreadability is important to ensure uniform distribution of active compounds across the wound area, thereby maximizing therapeutic effectiveness (Makrufa, 2025), (Iskandar et al., 2025).

### **In Vivo Wound Healing Activity**

The wound healing activity of the nanophytosome gel was evaluated using a diabetic rat wound model to determine its therapeutic potential in diabetic ulcer treatment. The results indicated that the treatment group receiving the nanophytosome gel containing combined extracts of *Syzygium polyanthum* and *Anredera cordifolia* showed a faster wound healing process compared to the control group.

The wound healing process was characterized by gradual reduction in wound size and the formation of new epithelial tissue in the wound area. These findings suggest that the formulation may significantly promote tissue regeneration during the wound healing process.

The therapeutic activity is likely associated with the presence of bioactive compounds such as flavonoids, saponins, and tannins found in both plant extracts. These compounds are known to possess antioxidant, anti-inflammatory, and antibacterial properties that are beneficial for wound healing. Flavonoids, in particular, play an important role in promoting angiogenesis and fibroblast proliferation, which are essential processes in tissue regeneration.

Furthermore, the nanophytosome delivery system enhances the penetration of phytochemical compounds into the skin, allowing more efficient delivery of active substances to the wound site. This improved penetration may contribute to the enhanced therapeutic effect observed in the treatment group (Rota Pramudiahwardani, 2025), (Al-fira, Garnadi, & Yani, 2024).

Overall, the results demonstrate that the nanophytosome-based gel formulation containing *Syzygium polyanthum* and *Anredera cordifolia* extracts has promising potential as an innovative topical therapy for diabetic wound management.

## **CONCLUSION**

The present study demonstrated that a nanophytosome-based delivery system containing a combination of *Syzygium polyanthum* and *Anredera cordifolia* extracts can be successfully developed and formulated into a topical gel preparation. The nanophytosome formulation showed favorable physicochemical characteristics, including appropriate particle size distribution, good stability, and satisfactory entrapment efficiency. The incorporation of nanophytosomes into a gel formulation produced a topical preparation with acceptable physical properties such as suitable pH, viscosity, and spreadability for skin application. In vivo evaluation indicated that the nanophytosome gel enhanced the wound healing process in diabetic wound models, as evidenced by faster wound contraction and improved tissue regeneration. These findings suggest that the nanophytosome gel containing *Syzygium polyanthum* and *Anredera cordifolia* extracts has promising potential as an innovative topical therapy for the management of diabetic foot ulcers. Further studies are recommended to evaluate its clinical efficacy and long-term safety.

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## References

- Adab, P. (n.d.). *Teknologi Biomaterial Maju Bagian 1: Prinsip, Klasifikasi, Dan Aplikasinya Dalam Sistem Pengantaran Obat Dan Pupuk*. Penerbit Adab.
- Akhsani, L. W. (2017). *Formulasi dan Uji Stabilitas Fisik-Kimia Sediaan Spray Gel Etil P-Metoksisinamat dari Rimpang Kencur (Kaempferia galangal Linn) dan Menthol*. Skripsi. Jakarta: UIN Syarif Hidayatullah Jakarta.
- Al-fira, P., Garnadi, J., & Yani, M. (2024). Pendekatan Sistem Penghantaran Nanopartikel Berbasis Lipid sebagai Obat Antijerawat: Review. *Pharmacoscrypt*, 7(2), 232-262.
- Anggraeni, S. N. (2023). Optimasi Konsentrasi CMC-Na dan Propilenglikol Terhadap Sifat Fisik Masker Gel Peel-off Ekstrak Kulit Putih Semangka Merah (*Citrullus lanatus*). Universitas dr. SOEBANDI.
- Aptika Oktaviana, T. D. (n.d.). ANALISIS KADAR KUERSETIN PADA EKSTRAK DENGAN METODE SPEKTROFOTOMETRI UV-VIS.
- Badaruddin, S., Rachmah, A. N. L., Ratumanan, R. C. F., Hukubun, R. D., & Trisnantari, T. C. (2025). Proses Ekstraksi Antioksidan dari Daun *Kalanchoe pinnata*: Studi Pengaruh Ukuran Partikel dan Kinetika Maserasi. *INSOLOGI: Jurnal Sains Dan Teknologi*, 4(4), 956-968.
- Bhayangkari, F. P. (2025). PENGARUH KOMBINASI PEMBERIAN SEDIAAN ORAL DAN TOPIKAL SALEP EKSTRAK ETANOL DAUN KITOLOD (*Isotoma longiflora* L.) TERHADAP PENYEMBUHAN LUKA SAYAT KELINCI NEW ZEALAND WHITE MODEL DIABETES INDUKSI ALOKSAN. Universitas Setia Budi.
- Girsang, B. M., Nasution, L. R., Ginting, K. H., & Elfira, E. (2025). *ETNOFARMAKOLOGI: PENGOBATAN HERBAL TRADISIONAL INDONESIA UNTUK PERAWATAN LUKA*. Azzia Karya Bersama.
- Haryanto, F. K., Jesica, I. A., Arafii, A. R., Pranasti, E. A., & Rosa, D. (2023). Review Jurnal: Pemanfaatan Daun Salam (*Syzygium polyanthum* (Wight) Walp.) Sebagai Pengobatan Tradisional di Indonesia. *PharmaCine: Journal of Pharmacy, Medical and Health Science*, 4(1), 20-33.
- Iskandar, B., Putri, A. H., Mardani, A. N., Putri, E. M., Tamba, E. C. U., Aulia, F., ... Utami, Z. R. (2025). Potensi Sediaan Nanogel dari Bahan Alami dalam Regenerasi Jaringan: Strategi Baru Pengobatan Luka Bakar. *Majalah Farmasetika*, 10(5).
- Lestari, P., Irfan, N., Indrayoni, P., Pristiyantoro, P., Rahmawati, N., Herli, M. A., ... Putri, N. (2025). *Teknologi Farmasi Bahan Alam*. PT. Sonpedia Publishing Indonesia.
- Maheswari, N. P. D. P. (2024). Peluang dan Tantangan Inovasi Sediaan Herbal Menggunakan Nanoteknologi untuk Pengobatan Herbal Modern di Indonesia. In *Prosiding Workshop dan Seminar Nasional Farmasi* (Vol. 3, pp. 74-87).
- Makrufa, S. A. S. (2025). Uji kualitas fisik dan biologi sediaan gel berbahan dasar ekstrak etanol kulit jeruk bali (*Citrus maxima*) terhadap hewan coba mencit. Universitas Islam Negeri Maulana Malik Ibrahim.
- Pulungan, D. R. A., Syahfitri, D., Adelia, D., & Salsabila, R. F. (2024). Daun salam (*Syzygium polyanthum*) rempah khas Indonesia dengan berbagai manfaat farmakologi: Literature review. *Indonesian Journal of Pharmaceutical Education*, 4(3).
- RANI, G. K. (2022). ENKAPSULASI FUKOSANTIN EKSTRAK ETANOL *Cyclotella striata* MENGGUNAKAN KITOSAN.
- RATUANIK, J. N. (2025). Hambatan Perawatan Kaki dan Praktik Keluarga dalam Mencegah Ulkus Kaki Diabetik di Komunitas Pulau Terpencil: Sebuah Studi Kualitatif= Barriers to Foot Care and Family Practices in Preventing Diabetic Foot Ulcers in Remote Island Communities: A Qualitative Study. Universitas Hasanuddin.
- Rismawati, R., Gondokesumo, M. E., & Aryani, N. L. D. (2025). Ulasan: Terapi Herbal untuk Penyembuhan Luka Ulkus Kaki Diabetik (Review: Herbal Therapy for Diabetic Foot Ulcer Wound Healing). *Jurnal*

- Surya Medika (JSM)*, 11(1), 1-16.
- Rosa Hanaya, C. (2025). Studi Formulasi dan Karakterisasi Nanofitosom dari Ekstrak Daun Salam (*Syzygium polyanthum*) serta Pengaruh Surfaktan Cremophor® Rh 40 sebagai Agen Penstabil. Universitas Bhakti Kencana.
- Rota Pramudiahwardani, A. (2025). Pengembangan Formula dan karakterisasi Nanoemulsi Menggunakan Ekstrak Daun Salam (*Syzygium polyanthum*) sebagai Agen Antikula. Universitas Bhakti Kencana.
- Setiawan, M. (2021). *Sistem endokrin dan diabetes mellitus*. UMMPress.
- Sholeha, N. A., Edi Wiraguna, S. P., Farobie, E. O., Melbi Mahardika, S. T., Jannah, D. M., Si, S. T., ... Atmaja, R. N. (n.d.). *Nanoteknologi Dalam Perspektif Pertanian Berkelanjutan: Inovasi Terkini Untuk Pertumbuhan Dan Proteksi Tanaman*. Penerbit Adab.
- Tomi, R. B., Nursoleha, E., & Febriyanti, A. D. (2025). Nanoenkapsulasi  $\beta$ -Sitosterol dengan Kombinasi Agen Enkapsulasi: Systematic Literature Review. *Jurnal Farmasi Aisyah*, 4(2), 157-171.
- Wiyanti, M. (2024). ASUHAN KEPERAWATAN PADA PASIEN DIABETES MELITUS TYPE II DENGAN HIPERGLIKEMIA MELALUI PEMBERIAN THERAPI INSULIN DI RUANG INSTALASI GAWAT DARURAT RS BHAYANGKARA TK I PUSDOKKES POLRI JAKARTA. Universitas Mohammad Husni Thamrin.
- Zubir, A. F., Brisma, S., Zulkarnaini, A., & Anissa, M. (2024). Gambaran Penderita Ulkus Diabetikum yang Menjalani Tindakan Operasi. *Scientific Journal*, 3(4), 232-241.