Proceedings Academic Universitas Jambi
Volume 1, Issue 2, November 2025

Enhancing the stability and retention of alkaloid compounds from gerga orange peel extract through nanoparticles: Potential application as a wound healing agent

Miftahurrahmah[1], Mirna Marhami Iskandar[2], Mara Imam Taufiq Siregar[3], Fitriyanti[1], Denok Tri Hardiningsih[3], Esa Indah Ayudia[2], Hafizah[2], Willy hardi Marpaung[1]

[1] Department of Surgery, Faculty of Medicine and Health Sciences, Jambi University, Jambi, Indonesia
[2] Department of Physiology, Faculty of Medicine and Health Sciences, Jambi University, Jambi, Indonesia
[3] Department of Phytopharmacy, Faculty of Medicine and Health Sciences, Jambi University, Jambi, Indonesia

*Coressponding Authors: Miftahurrahman_fkik@unja.ac.id, denoktrihardiningsih@unja.ac.id

Abstract

Background: Gerga orange peel (*Citrus* sp.) is a natural resource rich in alkaloid compounds, which have high pharmacological significance. However, these natural bioactive compounds are highly susceptible to degradation during the formulation and storage processes. **Objective:** This research aims to confirm the success of retention and evaluate the effectiveness of the nanoparticle formulation as an innovative strategy to protect and enhance the chemical stability of alkaloid compounds in Gerga orange peel extract. **Methods:** Gerga orange peel extract was formulated into a nanoparticle preparation using an appropriate method. The presence and retention of alkaloid compounds in the nanoparticle formulation were then qualitatively tested through comprehensive phytochemical screening. Testing was conducted using four standard alkaloid precipitating reagents: Dragendorff, Mayer, Bouchardat, and Wagner. Positive results in the reagent tests, characterized by the formation of typical precipitates, were used as an indicator of successful compound retention. **Results:** The Gerga orange peel extract nanoparticle preparation showed positive and consistent results in all four alkaloid reagent tests. This positive response is evidenced by the formation of characteristic precipitates in each test (orange-red precipitate with Dragendorff, white precipitate with Mayer, and brown precipitate with Bouchardat and Wagner). This finding definitively proves that the alkaloid compound was successfully maintained intact within the nanoparticle formulation matrix. **Conclusion:** The nanoparticle formulation proved to be a highly effective and superior strategy for preserving alkaloid compounds from Gerga orange peel. This successful retention of bioactive compounds ensures optimal integrity and pharmacological availability, opening up significant opportunities for further development of this extract into a stable and effective topical agent for wound healing applications.

Keywords: Alkaloid, Gerga orange peel, nanoparticles, preservation, retention, wound healing.

Cite This Article

Miftahurrahmah, Iskandar, M. M., Siregar, M. I. T., Fitriyanti, Hardiningsih, D. T., Ayudia, E. I., Hafizah, & Marpaung, W. H. (2025). Enhancing the stability and retention of alkaloid compounds from gerga orange peel extract through nanoparticles: Potential application as a wound healing agent. *Proceedings Academic Universitas Jambi*, *1*(2). 753-759.

Editor
I Made Dwi Mertha Adnyana, M.Ked.Trop.

Article info
Received: October 04, 2025. Revised: October 30, 2025. Accepted: November 09, 2025

INTRODUCTION

Nanoemulsions are highly effective in wound healing due to their ability to enhance skin permeation, provide controlled release, and stimulate fibroblast cell proliferation [1][2][3]. In recent studies on other citrus peels, such as *Citrus aurantium*, have demonstrated that peel-based ointments can accelerate wound healing by decreasing wound surface area and increasing muscle tensile strength[4][5][6] in addition, Orange peel extracts are rich in phenolic compounds, alkaloid, flavonoids, and carotenoids, which contribute to their high antioxidant activity [7][8][9]. these compounds are effective in scavenging free radicals, thus protecting cells from oxidative damage [10][11] [12]. Orange peel nanoemulsions also exhibit strong antibacterial properties, which are essential for preventing infections in wounds [13][14][15]. Therefore, Encapsulation of orange peel extracts in nanoemulsions enhances their antioxidant properties by providing better protection and controlled release of the bioactive compounds, This is beneficial for wound healing, and preventing infection. [11][13]

Although, there is no specific data on the orange peel from Gerga Kerinci, however various studies have demonstrated the wound healing and antioxidant properties of citrus peel extracts, including Citrus hystrix and Citrus aurantium[16] In addition, The molecular mechanisms by which orange peel nanoemulsions from Gerga Kerinci might promote wound healing and antioxidant effects are not detailed, while Existing studies on other citrus peels that have act in cell proliferation and migration [10]. However there is a lack of comparative studies evaluating the effectiveness of Gerga Kerinci orange peel nanoemulsion against but other citrus varieties For instance; Citrus aurantium peel-based ointments have shown promising results in wound healing [16] Accordingly, recent Studies on other citrus nanoemulsions indicate good stability and enhanced bioavailability whileThe stability and bioavailability of nanoemulsions containing Gerga Kerinci orange peel extract are not documented[17][1] Other studies have shown positive results for different citrus peels in animal models , but similar studies for Gerga Kerinci are needed to confirm its potential.[18]

Nanoemulsions enhance the stability and bioavailability of the active compounds. They provide a controlled release mechanism, ensuring a sustained therapeutic effect[1][17][19] Detailed mechanistic studies are required to understand the exact pathways through which orange peel nanoemulsions exert their wound healing and antioxidant effects. This study aims to develop and evaluate a nanoemulsion formulation of orange peel extract for topical wound healing. We hypothesize that encapsulating orange peel extracts in nanoemulsions will enhance their antioxidant and antibacterial properties, resulting in faster wound closure, and reduced infection rates compared to non-encapsulated extracts.

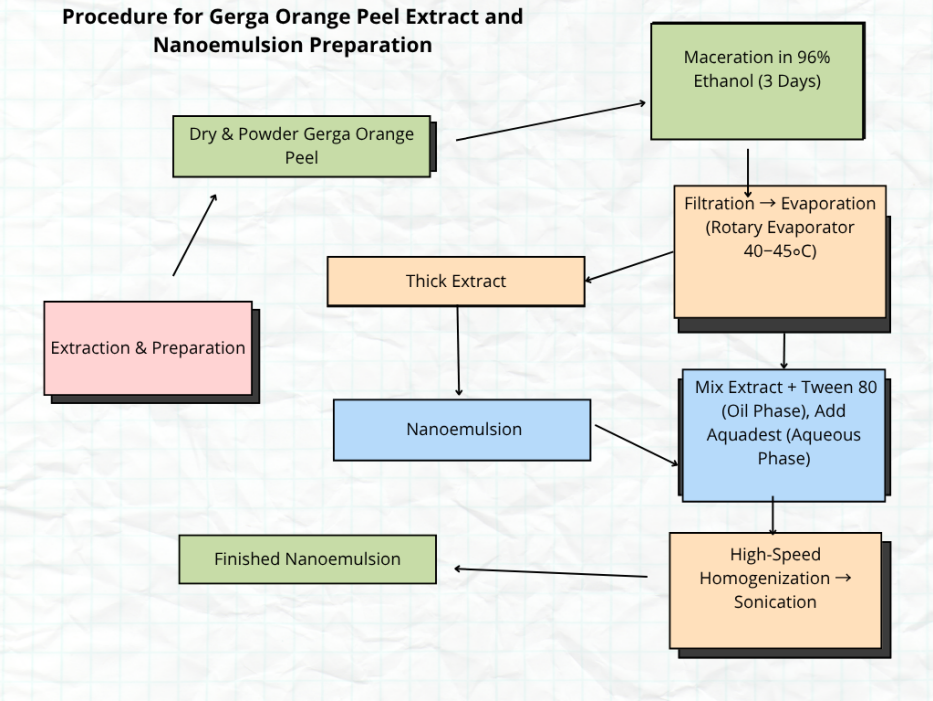
METHODS

Material and Method

Freshly harvested Gerga oranges kerinci from locally market in Jambi, Indonesia. Fresh oranges are washed to remove dirt and dust and then the peel is separated

from the pulp, juice, and seeds. After the skin is separated, it is cut into small pieces using a knife cutter. To remove the moisture content, the skin is dried in an oven dryer, at a temperature of about 50 ◦C for 6 hours and up to a humidity level of 4% d.b. The dry sample is then ground into a fine powder

The basic composition consists of active zak in the form of 4 mg of gerga kerinci orange peel ethanol extract, Tween 80 as a surfactant 8 ml, aquades as a solvent 68 ml. The manufacturing process begins by dissolving the extract into a portion of Tween 80 while stirring until homogeneous. The remaining Tween 80 and aquiades were added little by little while stirring using a homogenizer at 10,000–15,000 rpm for ±15 minutes. The mixture is then sonicated until a nanoemulsion with a particle size of 20–100 nm is formed with a polydispersivity index (PDI) of < 0.3. The nanoemulsion is stored in a dark glass bottle at room temperature. Analysis of the extract content in the nanoemulsion was carried out using UV–Vis spectrophotometry, and the results were used as the basis for determining the amount of nanoemulsion included in each ointment formula to be equivalent to the extract levels of 2.5 mg, 5 mg, and 7.5 mg.



Picture 1. Procedure for Gerga Orange Peel Extract and Nanoemulsion Preparation

RESULTS

Table 1. Table of the phytochemical test results for the Gerga orange peel nanoemulsion preparation:

No	Compound Group	Test Result	Description/Specific Test
1	**Flavonoids**	Positive	Formation of specific color change/reaction.
2	**Alkaloids**	Positive	- Dragendorff's Reagent: Positive (slight red precipitate). - Mayer's Reagent: Positive (white

No	Compound Group	Test Result	Description/Specific Test
			precipitate). - Bouchardat's Reagent: Positive (slight precipitate). - Wagner's Reagent: Positive (slight brown precipitate).
3	**Saponins**	Positive	Formation of stable foam.
4	**Phenolics**	Very Slightly Positive	Indicated by a light green color (changed to dark black in the extract, but very slight in the nanoemulsion).
5	**Steroids and Terpenoids**	Negative	Neither Steroids nor Terpenoids were detected.
6	**Quinones**	Positive	Indicated by a yellow/brick-red color.

DISCUSSION

Although no prior reports specifically addressed the orange peel from Gerga Kerinci, our phytochemical screening revealed the presence of flavonoids, alkaloids, saponins, phenolics, and quinones in its nanoemulsion extract, and an additional terpenoid component in the crude extract. The presence of flavonoids contributes to the antioxidant activity, which helps in neutralizing free radicals and reducing oxidative stress at the wound site. [20][21].

Moreover, Flavonoids, alkaloids, and terpenoids reduce the production of pro-inflammatory cytokines and enzymes, thereby decreasing inflammation and promoting a conducive environment for healing. [21][22]furthermore, The antimicrobial effects of alkaloids, saponins, and quinones help in preventing infections, which is crucial for effective wound healing. [22] lastly, collagen synthesis and angiogenesis effect of Saponins and flavonoids promote collagen synthesis and angiogenesis, which are essential for tissue repair and regeneration.[22] [20] Therefore, the phytochemical profile of Citrus reticulata var. Gerga Kerinci supports its potential as a novel wound-healing and antioxidant agent, aligning with previous findings from *Citrus hystrix* and *Citrus aurantium* extracts. [16]

Eventhough no comparative studies have directly evaluated *Citrus reticulata* var. *Gerga Kerinci* against other citrus species or standard wound-healing treatments, the present study provides initial evidence of its enhanced formulation performance. The nanoemulsion of Gerga Kerinci orange peel at 2.5% produced smaller particle sizes compared to the conventional extract at the same concentration, suggesting improved surface area, stability, and bioavailability of active compounds. [23]. This physicochemical advantage implies that nanoemulsion delivery could potentiate the wound-healing efficacy of Gerga Kerinci orange peel [24]. In addition, The active compounds in orange peel Gerga kerinci, when delivered via nanoemulsions, can suppress inflammatory cytokines, reduce oxidative stress, and enhance antioxidative enzymes, all of which are beneficial for wound healing.[24][25]

Although no direct evidence was obtained regarding wound infection in this study, the absence of infection signs throughout the experimental period suggests a potential antimicrobial or prophylactic effect of both the extract and the nano-emulsion formulations of *Gerga Kerinci* orange peel. [26][27] in recent study show that The antimicrobial properties of orange peel extracts suggest potential

applications in healthcare for treating infections and as additives in skincare products to combat acne and other skin infections[28][14] However in previous study showed that Orange peel methanolic extract (OPME) has been found to inhibit quorum sensing (QS) pathways in Pseudomonas aeruginosa, reducing biofilm formation and motility, which are critical for bacterial virulence [29] but in this study no microbiological assays were conducted, this potential remains undocumented. Future studies should therefore include bacterial culture or zone-of-inhibition assays to confirm whether the wound-healing benefits are partly mediated by infection prevention mechanisms.

CONCLUSIONS

Overall, the data showed that the formulation of Gerga orange peel extract nanoemulsion ointment at concentrations of 5 mg and 7.5 mg showed the most effective results in accelerating wound healing compared to other groups. This is supported by a small wound diameter on day 14, where all nanoemulsion formulas (2.5 mg [6.40±1.97 mm], 5 mg [7.55±3.56 mm], and 7.5 mg [7.40±3.59 mm]) showed better performance than Gentamycin's positive control (8.93±5.05 mm

CONFLICT OF INTEREST

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

FUNDING

This research was funded by the Bisma Fund from the LPPM of Jambi University.

ACKNOWLEDGMENT

The author would like to express gratitude to the LPPM of Jambi University for providing funds for the needs of this research.

DECLARATION OF ARTIFICIAL INTELLIGENCE USE

This study used artificial intelligence (AI) tools and methodologies in the following capacities Manuscript writing support: AI-based language models, such as [for example, ChatGPT, Quillbot], were/was employed to: Language refinement (improving the grammar, sentence structure, and readability of the manuscript), Content summarization (assisting in summarizing the findings and conclusions concisely), Technical writing assistance (providing suggestions for structuring complex technical descriptions more effectively), Generate scientific content, interpret data, and draw conclusions, Simulation and forecasting: Predictive modelling and simulations were conducted using AI frameworks to validate the research hypotheses. We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

REFERENCES

[1] Ben Amor I, Zeghoud S, Alnazza Alhamad A. Commentary on “Potential of nanoemulsions for accelerated wound healing: innovative strategies.” International Journal of Surgery (London, England) 2024;110:584–5. https://doi.org/10.1097/JS9.0000000000000772.

[2] Souto EB, Cano A, Martins-Gomes C, Coutinho TE, Zielińska A, Silva AM. Microemulsions and Nanoemulsions in Skin Drug Delivery. Bioengineering 2022;9:1–22. https://doi.org/10.3390/bioengineering9040158.

[3] Manohar G, Srivastava P. Translational potential of nanoemulsion in wound healing – From discovery to product commercialization. Next Nanotechnology 2025;7:100187. https://doi.org/10.1016/j.nxnano.2025.100187.

[4] Cherukuri S, Paramanayagam A, R P, M M, Vuppalapati L. Evaluation of Cutaneous Wound Healing Activity of Citrus aurantium Fruit Peel Extract-based Ointment in Albino Rats. Research Journal of Pharmacy and Technology 2023:250–4. https://doi.org/10.52711/0974-360X.2023.00046.
[5] Julaeha E, Puspita WR, Permadi N, Harja A, Nurjanah S, Wahyudi T, et al. Optimization of Citrus aurantifolia peel extract encapsulation in alginate-gelatin hydrogel microbeads for antibacterial wound dressing applications. Carbohydrate Polymer Technologies and Applications 2024;7:100406. https://doi.org/10.1016/j.carpta.2023.100406.
[6] Esra Karadag A, Demirci B, Şakar Zz, Biltekin Sn. Investigation of in vitro wound healing properties of Salvia sclarea and Citrus aurantium essential oil combinations. Journal of Research in Pharmacy 2024;28(5):1820–8. https://doi.org/10.29228/jrp.854.
[7] Kohli D, Sundriyal J, Kumar S, Upadhyay S, Hussain A. Investigating the antioxidant capacity of orange peel extract and its application in shelf-life extension of ghee. Journal of Stored Products Research 2024;107:102349. https://doi.org/10.1016/j.jspr.2024.102349.
[8] Lambangsari K, Regita AG, Munawaroh L, Simanjuntak EEY, Zafira ND, Abduh MY. Effects of fermentation time and extraction solvent on antioxidant activity and total phenolic and flavonoid content of phenolic extract from orange (Citrus reticulata) peel. IIUM Engineering J 2025;26:22–41. https://doi.org/10.31436/iiumej.v26i1.3173.
[9] Liu N, Li X, Zhao P, Zhang X, Qiao O, Huang L, et al. A review of chemical constituents and health-promoting effects of citrus peels. Food Chemistry 2021;365:130585. https://doi.org/10.1016/j.foodchem.2021.130585.
[10] Moolsup F, Tanasawet S, Woonnoi W, Daodee S, Parhira S, Chonpathompikunlert P, et al. Phytochemical analysis and impact of Citrus hystrix peel water extract on proliferation and migration of skin keratinocytes by activating FAK/Src/MAPK/Akt pathway. Journal of Herbal Medicine 2023;41:100699. https://doi.org/10.1016/j.hermed.2023.100699.
[11] Castro-Vázquez L, Lozano MV, Rodríguez-Robledo V, González-Fuentes J, Marcos P, Villaseca N, et al. Pressurized extraction as an opportunity to recover antioxidants from orange peels: Heat treatment and nanoemulsion design for modulating oxidative stress. Molecules 2021;26. https://doi.org/10.3390/molecules26195928.
[12] Mare R, Pujia R, Maurotti S, Greco S, Cardamone A, Coppoletta AR, et al. Assessment of Mediterranean Citrus Peel Flavonoids and Their Antioxidant Capacity Using an Innovative UV-Vis Spectrophotometric Approach. Plants 2023;12:1–15. https://doi.org/10.3390/plants12234046.
[13] Ikarini I, Fitriani F, Susanto JN, Nurcholis M, Winarti C, Lesmayati S, et al. Physicochemical and antibacterial activity on ultrasound-assisted nanoemulsions from different type of orange peel essential oil. Journal of Food Measurement and Characterization 2025;19:5041–52. https://doi.org/10.1007/s11694-025-03312-8.
[14] Rifka Alkhilyatul Ma'rifat, I Made Suraharta IIJ. Citrus aurantium L. peels and seeds: phytochemical screening and antibacterial activITY 2024;2:306–12.
[15] Mickky B, Elsaka H, Abbas M, Gebreil A, Eldeen RS. Plackett–Burman screening of physico-chemical variables affecting Citrus peel-mediated synthesis of silver nanoparticles and their antimicrobial activity. Scientific Reports 2024;14:1–17. https://doi.org/10.1038/s41598-024-58102-x.
[16] Cherukuri S, Paramanayagam A, R P, M M, Vuppalapati L. Evaluation of Cutaneous Wound Healing Activity of Citrus aurantium Fruit Peel Extract-based Ointment in Albino Rats. Research Journal of Pharmacy and Technology 2023:250–4. https://doi.org/10.52711/0974-360X.2023.00046.
[17] Rashid R, Wani SM, Manzoor S, Masoodi FA, Dar MM. Improving oxidative stability of edible oils with nanoencapsulated orange peel extract powder during accelerated

shelf life storage. Food Bioscience 2022;49:101917. https://doi.org/10.1016/j.fbio.2022.101917.
[18] Abbasi N, Ghaneialvar H, Moradi R, Zangeneh MM, Zangeneh A. Formulation and characterization of a novel cutaneous wound healing ointment by silver nanoparticles containing Citrus lemon leaf: A chemobiological study. Arabian Journal of Chemistry 2021;14:103246. https://doi.org/10.1016/j.arabjc.2021.103246.
[19] Kosksi T, Bustos-Salgado P, Selmi A, Rejeb M, Debbabi N, Espinoza LC, et al. Efficacy of Phlomis crinita Extract-Loaded Nanostructured Formulation in Accelerating Wound Healing. Pharmaceutics 2025;17:1–19. https://doi.org/10.3390/pharmaceutics17091093.
[20] Adhikary K, Sarkar R, Maity S, Sadhukhan I, Sarkar R, Ganguly K, et al. Immunomodulation of Macrophages in Diabetic Wound Individuals by Structurally Diverse Bioactive Phytochemicals. Pharmaceuticals 2024;17. https://doi.org/10.3390/ph17101294.
[21] Chanu NR, Gogoi P, Barbhuiya PA, Dutta PP, Pathak MP, Sen S. Natural Flavonoids as Potential Therapeutics in the Management of Diabetic Wound: A Review. Current Topics in Medicinal Chemistry 2023;23:690–710. https://doi.org/10.2174/1568026623666230419102140.
[22] Vitale S, Colanero S, Placidi M, Emidio G Di, Tatone C, Amicarelli F, et al. Phytochemistry and Biological Activity of Medicinal Plants in Wound. Molecules 2022;27:1–30.
[23] Manohar G, Srivastava P. Translational potential of nanoemulsion in wound healing – From discovery to product commercialization. Next Nanotechnology 2025;7:100187. https://doi.org/10.1016/j.nxnano.2025.100187.
[24] Rastogi V, Porwal M, Aalam A. A Review on Nanocarrier-based Polyherbal Drug Delivery Systems for Wound Healing. The Natural Products Journal 2024;14. https://doi.org/10.2174/0122103155294431240129063752.
[25] Jessy Mercy D, Thirumalai A, Udayakumar S, Deepika B, Janani G, Girigoswami A, et al. Enhancing Wound Healing with Nanohydrogel-Entrapped Plant Extracts and Nanosilver: An In Vitro Investigation. Molecules 2024;29. https://doi.org/10.3390/molecules29215004.
[26] Hajialyani M, Tewari D, Sobarzo-Sánchez E, Nabavi SM, Farzaei MH, Abdollahi M. Natural product-based nanomedicines for wound healing purposes: Therapeutic targets and drug delivery systems. International Journal of Nanomedicine 2018;13:5023–43. https://doi.org/10.2147/IJN.S174072.
[27] Mohamed NK, Metwally AA, Fared SMY, Farid A, Taha M. Formulation and characterization of tea tree and jojoba oils nano-emulgel for in-vivo wound healing assessment. Colloids and Surfaces B: Biointerfaces 2025;245:114312. https://doi.org/10.1016/j.colsurfb.2024.114312.
[28] Ibrar M, Ayub Y, Nazir R, Irshad M, Hussain N, Saleem Y, et al. Garlic and ginger essential oil-based neomycin nano-emulsions as effective and accelerated treatment for skin wounds' healing and inflammation: In-vivo and in-vitro studies. Saudi Pharmaceutical Journal 2022;30:1700–9. https://doi.org/10.1016/j.jsps.2022.09.015.
[29] Jaiswal S, Gaur SS. Orange Peel and Skin Health: An Exploratory Study on Potential Benefits. Journal of Food Chemistry and Nanotechnology 2023;9:S91–9. https://doi.org/10.17756/jfcn.2023-s1-013.
[30] Kumar L, Patil P, Bisen M, Srivastava N, Thakur D. Citrus sinensis fruit peel phytochemicals inhibit Pseudomonas aeruginosa biofilms and suppress motility phenotypes by potentially targeting quorum sensing pathways. South African Journal of Botany 2024;174:152–66. https://doi.org/10.1016/j.sajb.2024.08.052.