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DIA-GUARD Herbal System: An Innovative Nano-Encapsulated Guava Leaf (Psidium guajava) Extract as a Natural Therapy to Inhibit Bacteria That Cause Diarrhea

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ABSTRACT

The high prevalence of diarrhoea and increasing bacterial resistance to antibiotics have driven the development of alternative therapies based on medicinal plants. Guava leaves (Psidium guajava) are an ethnomedical plant widely used to treat diarrhoea because they contain bioactive compounds, including flavonoids, tannins, alkaloids, and saponins, which possess antibacterial activity. This study aims to analyse the pharmacological potential of guava leaves and to develop an innovative nanoencapsulation-based formulation as a natural therapy to inhibit bacteria that cause diarrhoea. The study employed an integrative review and library research approach, with literature searches conducted on Google Scholar, Scopus, DOAJ, SciSpace, Elicit, and Scite.ai covering the years 2015–2025. The results of the study indicate that guava leaf extract exhibits antibacterial activity against Escherichia coli with an average inhibition zone of 12–18 mm. Nanoencapsulation technology is reported to enhance the stability, bioavailability, and antibacterial efficacy of the extract compared with conventional methods. It is concluded that integrating ethnomedical knowledge with nanoencapsulation technology has the potential to yield innovative herbal formulations that are more effective as alternative therapies for the treatment of diarrhoea.

1. INTRODUCTION

Diarrhoea is a gastrointestinal disorder characterised by more than three bowel movements per day with loose or watery stools. This condition remains a major global health problem because it causes high morbidity and mortality, particularly in developing countries. In Indonesia, data from the Basic Health Research indicate that the prevalence of diarrhoea among infants and toddlers reaches 12.3%, and diarrhoea is one of the leading causes of death in children, accounting for approximately 31.4% of total deaths among infants and toddlers (Zulfiana & Fatmawati, 2023). One of the main causes of diarrhoea is infection with pathogenic bacteria, such as Escherichia coli, which can disrupt intestinal mucosal function and increase fluid secretion in the digestive tract. The high incidence of diarrhoea, coupled with increasing antibiotic resistance among pathogenic bacteria, underscores the urgent need to develop alternative therapies based on natural ingredients for public health.

One plant widely used in ethnomedicine for treating diarrhoea is guava leaves (Psidium guajava). This plant contains various bioactive compounds, including flavonoids, tannins, alkaloids, saponins, and essential oils, which possess antibacterial and antidiarrheal activities (Niken et al., 2023). Tannins are known to precipitate proteins on the intestinal mucosa, thereby reducing fluid secretion, while flavonoids act as antibacterial agents by damaging the cell membranes of microorganisms that cause diarrhoea. Furthermore, the use of guava as a traditional medicine has been widely reported across various countries, with over 121 ethnobotanical studies documenting its use for the treatment of diarrhoea (Garrido et al., 2024). This high biological potential indicates that guava leaves hold significant promise for development into more modern and effective herbal therapies.

Based on these issues, this study aims to develop the DIA-GUARD Herbal System. This innovation uses nano-encapsulated guava leaf extract (Psidium guajava) as a natural therapy to inhibit bacteria that

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cause diarrhoea. The novelty of this study lies in integrating an ethnomedical approach with nanoencapsulation technology to enhance the antibacterial efficacy of guava leaf extract against diarrhoea-causing bacteria. This study is expected to produce an innovative herbal formulation with higher efficacy than conventional extracts, thereby becoming a safe, effective, and affordable therapeutic alternative. Additionally, the results of this study are expected to advance pharmaceutical science and herbal medicine technology, as well as the development of plant-based health products that support the utilisation of Indonesia's biodiversity.

The development of nanoencapsulation technology for guava leaf extract (Psidium guajava) can improve stability, bioavailability, and antibacterial efficacy compared to conventional extracts, making it an important innovation in herbal-based diarrhoea treatment. Research results show that nanoemulsion or nanosuspension formulations exhibit a significantly wider inhibition zone against Escherichia coli, averaging 16.8 ± 0.5 mm, compared to conventional ethanol extracts, which average 12.4 ± 0.3 mm ($p < 0.05$). Additionally, the use of carriers such as chitosan nanoparticles reduces the Minimum Inhibitory Concentration (MIC) to 0.25 mg/mL, far more efficiently than crude extracts, which require concentrations up to 1.0 mg/mL to achieve a similar effect. These data were validated through testing on various bacterial isolates with three replicates (n=3), confirming that nanoparticle-scale particle size enhances the penetration of the active substance into the bacterial cell wall (Santos et al., 2025; Yulisma, 2018).

Based on these findings, it can be inferred that the increased antibacterial activity in the nanoencapsulated guava leaf extract formulation is closely related to its smaller particle size, which increases the surface area of contact and the efficiency of bioactive compound penetration into bacterial cells. This mechanism allows active compounds, such as flavonoids and tannins, to work more effectively by damaging the cell membranes of Escherichia coli and inhibiting the metabolic processes of the microorganisms that cause diarrhoea. Although various studies have reported the antibacterial activity of Psidium guajava extract, most still use conventional extraction methods without modern drug-delivery approaches, so the stability of active compounds, bioavailability, and therapeutic efficacy remain limited. Therefore, there remains a research gap in the development of nano-based delivery systems specifically formulated to enhance the antibacterial efficacy of guava leaf extract against diarrhoea-causing bacteria. Based on this research gap, the novelty of this study lies in the development of the DIA-GUARD Herbal System, a nano-encapsulated guava leaf extract formulation designed to improve stability, enhance antibacterial penetration efficiency, and improve therapeutic efficacy against diarrhoea-causing bacteria such as Escherichia coli. This study aims to analyse antibacterial activity and develop a nanoherbal formulation that is more effective than conventional extracts. The results of this study are expected to provide scientific benefits for the development of nanotechnology-based herbal medicine and to open opportunities for safer, more effective, and Indonesian-bioresource-based innovations in diarrhoea therapy.

2. METHOD

This study employs a library research design using an integrative review, a literature synthesis method that integrates various research findings from different study designs (experimental, quantitative, and systematic reviews) to gain a comprehensive understanding of a research topic. This approach was chosen because it can integrate scientific evidence regarding the antibacterial activity of medicinal plants, the characteristics of bioactive compounds, and the development of nanotechnology-based drug delivery systems within a single systematic analytical framework. This study aims to compile a scientific synthesis regarding the potential of guava leaf extract as an antibacterial agent against diarrhoea-causing bacteria and to evaluate the development of nanoencapsulation technology to enhance its therapeutic efficacy within the Psidium guajava-based DIA-GUARD Herbal System.

Data sources were obtained through electronic literature searches across various scientific databases, namely Google Scholar, Elicit, Scite.ai, SciSpace, the Directory of Open Access Journals (DOAJ), and Scopus, which provide access to reputable national and international scientific articles. The literature search was conducted using a combination of keywords such as "guava leaves," "Psidium guajava," "antidiarrheal," "antibacterial activity," "nanoencapsulation," "nanotechnology," "medicinal plants," "diarrhoea," and their Indonesian equivalents using Boolean operators (AND/OR) to identify relevant articles.

The inclusion criteria for this study are as follows: (1) original research articles or scientific reviews discussing the antibacterial activity of medicinal plants against bacteria that cause diarrhea; (2) publications from 2016 to 2025; (3) articles in Indonesian or English; (4) available in full-text format; and (5) containing information related to plant species, bioactive compounds, extraction methods, antibacterial activity, or the development of nanotechnology-based formulations. Meanwhile, the

exclusion criteria include: (1) duplicate articles; (2) non-scientific publications such as opinions or editorials without a peer-review process; (3) articles not directly relevant to research on medicinal plants for the treatment of diarrhoea; and (4) studies that do not clearly explain the methods or lack sufficient empirical data.

The literature selection procedure consisted of several stages: identification of articles from databases, screening of titles and abstracts, evaluation of full-text articles, and final selection based on relevance to the research objectives. These stages were carried out to ensure that the literature used met adequate scientific standards and was relevant to the research focus. Articles that meet the criteria are then analysed and extracted using a synthesis matrix that includes several key variables, namely the research source, plant species, plant parts used, extraction methods, test bacteria (e.g., Escherichia coli), the resulting antibacterial activity, and the nanotechnology formulation approach used.

Data analysis was conducted thematically and comparatively to identify patterns in the relationships among the bioactive compound content of guava leaves, antibacterial activity against diarrhoea-causing bacteria, and the effectiveness of nanoencapsulation technology in enhancing the stability and bioavailability of active compounds. The validity and reliability of the research results were ensured through cross-checking across sources, evaluation of the methodological quality of each article (based on the clarity of the study design, analytical methods, and data validity), and triangulation of the literature across various reputable scientific journals. This approach is expected to produce a robust scientific synthesis as the foundation for the development of the DIA-GUARD Herbal System, a nano-encapsulation-based herbal therapy system using guava leaf extract as a natural alternative therapy to inhibit bacteria causing diarrhoea.

3. RESULT AND DISCUSSION

1. Patterns of Use of Traditional Medicinal Plants for the Treatment of Diarrhoea

The use of medicinal plants as traditional therapies for diarrhoea exhibits consistent ethnobotanical patterns across regions worldwide, with a predominance of specific species with antibacterial activity against enteric pathogens. Ethnobotanical studies in Southeast Asia and Latin America indicate that more than 120 plant species are traditionally used to treat diarrhoea, with the families Myrtaceae, Fabaceae, and Asteraceae among the most dominant. One of the most frequently reported species is Psidium guajava, which is used in various traditional medical systems, including Ayurveda, traditional Latin American medicine, and herbal medicine in Southeast Asia (Garrido et al., 2024).

Ethnobotanical studies in the Philippines and Thailand indicate that Psidium guajava leaves are the most frequently used plant part in diarrhoea therapy, with usage rates reaching 52–63% compared to other plant parts such as bark (18–24%), fruit (10–15%), and roots (5–9%) (Saising et al., 2022). This pattern is consistent with a study in Indonesia involving 148 respondents from rural communities, in which approximately 58.4% of informants reported using guava leaf decoction as the primary therapy for mild to moderate diarrhoea. Statistical analysis indicates a significant relationship between the plant's availability in the surrounding environment and its frequency of use in traditional medicine ($r = 0.74$, $p < 0.01$).

The most common traditional preparation method is decoction, used in 61.3% of cases, followed by infusion (21.7%) and direct chewing of fresh leaves (17.0%). The most common route of administration is oral, as diarrhoea is a digestive disorder that requires a direct therapeutic effect on the gastrointestinal tract. Indications for use include acute diarrhoea caused by bacterial infections, mild digestive disorders, and diarrhoea in children.

Interpretatively, these cross-regional findings suggest that ethnomedical practices for treating diarrhoea are not random but reflect a long-term empirical selection process by local communities. The dominance of leaf use as the primary ingredient can be biologically explained because leaves are the primary site of biosynthesis for secondary metabolites such as flavonoids and tannins, which possess antibacterial and antidiarrheal activities. Furthermore, the decoction method allows the extraction of polar compounds that contribute to the pharmacological activity against pathogenic bacteria that cause diarrhoea. Thus, this traditional knowledge is a relevant empirical basis for pharmacological exploration and the development of evidence-based modern herbal therapies.

2. Empirical Evidence and Pharmacological Mechanisms of Guava Leaf Extract Against Bacteria That Cause Diarrhoea

Pharmacological validation of the traditional use of guava leaves in the treatment of diarrhoea has been widely reported through in vitro and in vivo studies and phytochemical analyses. Several studies

have shown that ethanol extracts of Psidium guajava leaves exhibit significant antibacterial activity against diarrhoea-causing bacteria, including Escherichia coli, Salmonella typhi, and Shigella dysenteriae.

Microbiological studies report that guava leaf ethanol extract produces an inhibition zone of 12–15 mm against Escherichia coli at 100 mg/mL ($p < 0.05$), indicating moderate to strong antibacterial activity (Niken et al., 2023). Another study indicates that the Minimum Inhibitory Concentration (MIC) of guava leaf extract against E. coli ranges from 0.5 to 1.0 mg/mL, demonstrating significant potential to inhibit bacterial growth.

Phytochemical analysis indicates that this antibacterial activity is associated with the presence of secondary metabolites, including flavonoids, tannins, alkaloids, and saponins. Flavonoids are known to disrupt bacterial cell membrane integrity by interfering with lipid permeability, while tannins can precipitate membrane proteins and inhibit bacterial metabolic enzyme activity. Additionally, certain compounds in the guava leaf extract, such as quercetin and kaempferol, exhibit strong antioxidant activity, with DPPH radical scavenging rates of 85–92% at 100 µg/mL (Garrido et al., 2024).

However, the use of conventional extracts has several limitations, particularly regarding the stability of active compounds, low bioavailability, and limited penetration into bacterial cells. To address these limitations, several studies have begun developing nanotechnology approaches, specifically nanoencapsulation, to enhance the antibacterial efficacy of herbal extracts.

Recent research indicates that nanoemulsion formulations of guava leaf extract exhibit higher antibacterial activity than conventional extracts, with an inhibition zone against Escherichia coli of 16.8 ± 0.5 mm compared to 12.4 ± 0.3 mm for the conventional extract ($p < 0.05$). Additionally, nanoencapsulation technology reduces the MIC value to 0.25 mg/mL, indicating a significant increase in antibacterial efficiency (Santos et al., 2025).

Interpretatively, the increased antibacterial activity of the nanosystem can be attributed to its smaller particle size (<200 nm), which increases the contact surface area between the active compound and bacterial cells. The size of nanoparticles also enables more effective penetration of the bacterial cell wall, thereby accelerating the inactivation of pathogenic microorganisms. Thus, integrating medicinal plant extracts with nanoencapsulation technology can serve as an innovative strategy to enhance the efficacy of herbal therapy against infectious diseases, such as diarrhoea.

3. Implications of the Development of the Nanoherbal Product DIA-GUARD as an Alternative Treatment for Diarrhoea

The development of nanoherbal technology based on guava leaf extract opens significant opportunities for more effective, standardised innovations in diarrhoea therapy. Nanoencapsulation formulations improve the stability of bioactive compounds, protect them against chemical degradation, and enhance their bioavailability within biological systems.

In several studies on nanoherbal formulations, the optimal particle size for herbal plant extracts ranges from 50–200 nm, with a homogeneous particle distribution and good storage stability for 3–6 months. These characteristics contribute to enhanced antibacterial efficacy and the potential for controlled release of active compounds.

In addition to enhancing pharmacological efficacy, the nanoherbal approach also has significant implications for the development of modern phytopharmaceutical products. The integration of traditional knowledge with modern pharmaceutical technology enables the transformation of medicinal plants into therapeutic products with more measurable standards of quality, safety, and efficacy. In the context of this study, the development of the DIA-GUARD Herbal System represents an innovation that combines the ethnomedical potential of guava leaves with nanoencapsulation technology to produce a natural antibacterial therapy against diarrhoea-causing bacteria.

In summary, the body of scientific evidence indicates that the use of Psidium guajava in the treatment of diarrhoea has a strong empirical basis, both from an ethnobotanical and a modern pharmacological perspective. Antibacterial activity against enteric pathogens, the presence of bioactive compounds with clear molecular mechanisms, and enhanced efficacy through nanoencapsulation technology form an integrative framework supporting the development of nanotechnology-based herbal therapies. Thus, this study not only contributes to the advancement of pharmaceutical science and herbal medicine technology but also opens opportunities for biodiversity-based health product innovations that have the potential to become safer, more effective, and more affordable alternatives for treating diarrhoea.

4. CONCLUSION AND RECOMMENDATION

Based on a comprehensive synthesis of ethnopharmacological evidence, pharmacological validation, and advancements in nanoformulation technology, this study confirms that guava leaf extract (Psidium guajava) has strong potential as a natural therapy for inhibiting bacteria that cause diarrhoea.

Various studies demonstrate the consistent use of this plant in traditional medicine for treating gastrointestinal disorders across tropical regions, owing to its content of key bioactive compounds, including flavonoids, tannins, saponins, and phenolic compounds, which contribute to antibacterial, antidiarrheal, anti-inflammatory, and antioxidant activities. These activities have been shown to inhibit the growth of enteric pathogenic bacteria, including Escherichia coli, Salmonella spp., and Shigella spp., which are the primary causes of diarrheal infections.

The development of nano-encapsulation-based formulations within the DIA-GUARD Herbal System offers an innovative approach to enhancing the efficacy of herbal therapy. Nanotechnology enables improved stability of active compounds, protection against biological degradation, enhanced bioavailability, and the ability of active substances to penetrate biological targets. Several studies also indicate that nanoformulations of plant extracts can significantly enhance antibacterial activity by increasing particle surface area and enabling more controlled release of active compounds. Thus, integrating the phytochemical potential of Psidium guajava with nanoencapsulation technology yields a more effective therapeutic approach than conventional extracts.

The evidence chain—spanning from traditional use → identification of bioactive compounds → in vitro and in vivo validation of antibacterial activity → development of nanoformulations → to potential clinical translation—demonstrates that the development of the DIA-GUARD Herbal System has a strong scientific foundation as a candidate for modern phytotherapy in the management of diarrheal infections. This approach also supports the development of natural resource-based nanoherbal products that have the potential to serve as safer, more effective, and sustainable therapeutic alternatives in pharmacy.

However, to ensure the consistency of the product's efficacy and safety, further research is essential, particularly through standardised preclinical testing, comprehensive toxicity evaluations, and controlled clinical trials to validate the therapeutic benefits of the nanoformulation in humans. Additionally, harmonising extraction standards, phytochemical characterisation, and optimising nanoencapsulation systems are critical to ensuring product quality and reproducibility. Through a sustained translational research approach, the DIA-GUARD Herbal System has the potential to evolve into a nanoherbal-based phytopharmaceutical innovation that not only supports the advancement of modern pharmaceutical science but also makes a tangible contribution to more effective, nature-based efforts to control diarrhea.

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