



Potential Effectiveness of Goji Berry (*Lycium barbarum L.*) Extract on Neutrophil Cell Count in Wistar Rats (*Rattus norvegicus*) Post Tooth Extraction

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Abstract: Tooth extraction causes tissue injury that triggers an inflammatory response, which is characterized by an increase in neutrophil counts. Although neutrophils play an essential role in the early phase of wound healing, prolonged inflammation may delay tissue regeneration. Goji berry (*Lycium barbarum L.*) contains various bioactive compounds that have potential anti-inflammatory effects. This study aimed to evaluate the effectiveness of goji berry extract on neutrophil counts in Wistar rats (*Rattus norvegicus*) following tooth extraction. This study was experimental laboratory research using a post-test group design. A total of 30 male Wistar rats were divided into five groups: negative control, positive control (povidone iodine), and three treatment groups receiving goji berry extract at concentrations of 15%, 30%, and 55%. The extract was formulated as a gel and applied topically to the extraction socket. Neutrophil counts were evaluated on days 1, 3, 5, and 7 through histopathological examination. Data were analyzed using the Shapiro-Wilk test, One Way ANOVA, and the LSD post hoc test. The results showed significant differences in neutrophil counts among groups on days 3, 5, and 7 ($p < 0.05$). The 55% concentration demonstrated the most optimal reduction in neutrophil counts. It can be concluded that goji berry extract has potential as an alternative herbal therapy to support wound healing after tooth extraction.

Keywords: Goji berry; *Lycium barbarum L.*; Neutrophils; Tooth extraction; Wound healing

Introduction

Oral and dental health remains a critical issue requiring serious attention, given the high prevalence of dental and oral diseases in the community. Various reports indicate that dental and oral disorders not only impact masticatory function, phonetics, and aesthetics, but also have the potential to reduce a person's overall quality of life. Based on Basic Health Research (Riskesdas) data, tooth extraction is recorded as one of the most commonly performed treatment procedures by dentists and is widely accepted by the public. This high rate of tooth extraction reflects the limited prevention efforts and delayed treatment of dental diseases, resulting in many cases being untreatable and ultimately

resulting in extraction. In principle, tooth extraction should be a last resort if the tooth is no longer treatable and can no longer be preserved (Rahmawati et al., 2023).

Tooth extraction is defined as the process of removing a tooth from its socket or alveolar process. This procedure directly causes damage to the surrounding tissues, including both hard and soft tissues, resulting in a wound at the extraction site (Prestiyanti et al., 2021). Post-tooth extraction wounds require a complex healing process so that the tissues can return to normal function through the formation of new tissue. Wound healing is a series of biological mechanisms involving various cells, mediators, and tissues, aimed at repairing tissue damage and restoring

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impaired function resulting from injury (Rahmawati et al., 2023).

Physiologically, the wound healing process occurs through four main stages: hemostasis, inflammation, proliferation, and maturation. The inflammatory stage is the body's initial response to injury, lasting for 1–2 days, and plays a crucial role in determining the success of subsequent healing processes (Oki & Amalia, 2020). During the inflammatory phase, the body works to clear the wound area of infection-causing microorganisms as well as remnants of damaged tissue. This process begins with the migration of leukocytes, particularly neutrophils, to the wound site. Neutrophils act as the first line of defense by eliminating bacteria and fungi through mechanisms such as phagocytosis, degranulation, and the release of Neutrophil Extracellular Traps (NETs). Although neutrophils play a vital role in preventing infection, excessive or prolonged neutrophil presence can lead to tissue damage and prolong the inflammatory phase. Therefore, regulating the number and activity of neutrophils is an important factor in maintaining a balance between immune responses and tissue regeneration processes (Azizah et al., 2024).

In clinical practice, to prevent infection and control inflammation after tooth extraction, dentists generally prescribe certain medications. Commonly used drugs include Non-steroidal Anti-Inflammatory Drugs (NSAIDs) to reduce pain and inflammation, povidone iodine as a topical antiseptic, and CMC-Na in gel form to help maintain wound moisture. However, the use of these medications is not without the risk of side effects. Povidone iodine, for example, has irritant properties and may be potentially toxic if it enters the bloodstream. In addition, excessive use of povidone iodine can inhibit the growth of granulation tissue, which may actually delay the wound healing process (Azizah et al., 2024). This condition indicates the need for alternative therapies that are safer, effective, and associated with minimal side effects to support wound healing after tooth extraction.

Along with the increasing public awareness of the side effects of synthetic drugs, the use of herbal medicines has become an increasingly popular option. Herbal-based therapies, particularly those applied topically, have been shown to be effective in accelerating the wound healing process. In addition to their effectiveness, herbal therapies are considered safer because they cause minimal side effects, making them suitable as alternatives or adjunctive therapies to synthetic chemical drugs. Herbal medicines offer advantages such as easy availability of raw materials, relatively affordable costs, and a higher safety profile compared to synthetic drugs (Djuma & Kurnia, 2024).

Studies also emphasize that natural bioactive compounds in medicinal plants play a role in accelerating tissue regeneration and suppressing inflammatory responses, thereby supporting optimal wound healing with a lower risk of side effects. Therefore, the exploration of herbal plants as wound-healing agents is a relevant and important research topic to be further developed (Istiqomah et al., 2024).

One herbal plant with great potential in the health field is goji berry (*Lycium barbarum L.*). Goji berry is not only known as a tonic food but has also long been used in traditional medicine due to its wide range of health benefits, including improving lung function, nourishing the blood, enhancing vision, and accelerating wound healing. The main nutritional components of goji berry are polysaccharides rich in vitamin C, along with various essential minerals such as potassium, copper, manganese, iron, and zinc. These minerals play a role in regulating mineral metabolism and maintaining tissue osmotic pressure balance, which is crucial in the tissue regeneration process. In addition, goji berry (*Lycium barbarum L.*) contains carotenoids that act as bioactive constituents. Other bioactive compounds present include amides, flavonoids, organic acids, and lignanoids, which are known to exhibit antioxidant, anti-inflammatory, and immunomodulatory activities (Cui et al., 2022).

Based on its bioactive constituents, goji berry (*Lycium barbarum L.*) has the potential to be developed as an alternative agent to accelerate wound healing after tooth extraction. In addition to its biological potential, goji berry is relatively easy to obtain in Indonesia through herbal medicine stores, online sales platforms, and supermarkets, providing broad prospects for clinical application. To enhance its effectiveness for topical use on oral mucosal tissues, goji berry extract can be formulated in a gel dosage form. Gel formulations offer advantages such as a cooling effect on the mucosal tissue, the ability to maintain wound moisture, and reduced irritation due to their high water content, thereby supporting patient comfort and therapeutic effectiveness (Halim et al., 2021).

Although various studies have reported the general health benefits of goji berry, its use as an alternative herbal medicine for wound healing after tooth extraction remains very limited. To date, goji berry (*Lycium barbarum L.*) has not been widely used or specifically studied as a wound-healing agent following tooth extraction, particularly in relation to the inflammatory response indicated by neutrophil cell counts in Wistar rats (*Rattus norvegicus*). In fact, the evaluation of neutrophil cell numbers is an important indicator for assessing the level of inflammation and the effectiveness of an agent in supporting the wound healing process.

Therefore, the novelty of this study lies in the exploration of the potential effectiveness of goji berry extract (*Lycium barbarum L.*) formulated as an alternative agent for post-tooth extraction wound healing, with a particular focus on its effect on neutrophil cell counts as an indicator of the inflammatory phase. This study is expected to provide new scientific contributions to the development of herbal therapies in the field of dentistry, especially as a safer and more effective alternative for controlling post-extraction inflammation in Wistar rats (*Rattus norvegicus*), and to serve as a foundation for further research and future clinical applications.

Method

This study was a laboratory-based experimental study employing a post-test group design. The research was conducted from July to November 2025 across several laboratories: the Herbarium Laboratory of Universitas Sumatera Utara for plant determination; the Research and Development Laboratory of Aspetri Medicinal Plants for extract preparation and gel formulation; the Basic Science Laboratory of Universitas Prima Indonesia for phytochemical analysis; and the Microbiology Laboratory and the Integrated Laboratory of the Faculty of Medicine, Universitas Sumatera Utara, for the maintenance of experimental animals and the examination of neutrophil cell counts.

Research Subjects and Treatment Design

The research subjects were male Wistar strain rats (*Rattus norvegicus*), aged 2–3 months, with body weights ranging from 150 to 200 grams. The experimental animals were selected using purposive sampling based on predefined inclusion and exclusion criteria. The rats were in healthy condition, had no history of infectious disease, and were able to survive throughout the study period. Rats that developed infections outside the tooth extraction socket, sustained injuries that could affect the study outcomes, or did not survive during the experimental period were excluded from the analysis.

The sample size was determined using Federer's formula, with five treatment groups and a minimum of five rats per group. A total of 30 rats were used in this study and were divided into five groups: a negative control group (no treatment), a positive control group (povidone iodine), and three treatment groups receiving Goji berry (*Lycium barbarum L.*) extract at concentrations of 15%, 30%, and 55%.

Preparation of Goji Berry Extract and Gel Formulation

Goji berry fruits (*Lycium barbarum L.*) were obtained from Lautan Timur Chinese Pharmacy, North Sumatra,

and taxonomic identification was performed to confirm their botanical identity. The fruits were washed, dried at 40 °C, and ground into fine powder. Extraction was carried out using the maceration method with 96% ethanol as the solvent for 5–10 days with periodic stirring. The resulting filtrate was evaporated at 50 °C to obtain a concentrated extract. The extract was then formulated into a gel using sodium carboxymethyl cellulose (Na-CMC) as the gel base. Phytochemical screening was conducted to identify the presence of active compounds, including alkaloids, flavonoids, saponins, and tannins.

Experimental Animal Treatment Procedure

Prior to treatment, the rats were acclimatized for one week under a 12-hour light-dark cycle and were provided with standard feed and drinking water. The rats were then anesthetized using ketamine at a dose of 20–40 mg/kg body weight administered intraperitoneally. Extraction of the mandibular incisor was performed using standard dental instruments, ensuring that no root remnants remained. Following tooth extraction, the Goji berry extract gel was applied topically into the tooth socket using a syringe according to the respective treatment groups. The application was carried out twice daily at 12-hour intervals for seven consecutive days.

Sample Collection and Neutrophil Examination

Tissue samples were collected on days 1, 3, 5, and 7 following tooth extraction. Histopathological tissue preparations were examined to quantify neutrophil cell counts using a phase-contrast inverted microscope at 400× magnification and analyzed with Image Raster 3.0 software. After completion of all experimental procedures, the animals were humanely euthanized in accordance with established ethical standards for animal research.

Data Analysis

Neutrophil cell count data were analyzed using the Shapiro-Wilk normality test. Data that were not normally distributed were analyzed using the Kruskal-Wallis and Mann-Whitney tests, whereas data that were normally distributed and homogeneous were analyzed using one-way analysis of variance (ANOVA), followed by the Least Significant Difference (LSD) post hoc test. A p-value of < 0.05 was considered statistically significant.

Result and Discussion

Result

Plant determination was carried out at the Herbarium Medanense, Universitas Sumatera Utara, to

confirm the identity of the plant material used in this study. The identification results showed that the plant belongs to the Kingdom Plantae, Division Spermatophyta, Class Dicotyledoneae, Order Solanales, Family Solanaceae, Genus Lycium, and Species *Lycium barbarum L.*, with the local name Goji berry. Based on these findings, it can be confirmed that the goji berry fruits used in this study were derived from the species *Lycium barbarum L.* Furthermore, phytochemical screening was conducted to determine the presence of active compounds in the Goji berry extract, with the complete results presented in Table 1.

Table 1. Phytochemical Screening Results of Goji Berry

Secondary metabolites	Reagent	Result
Flavonoids	Mg(s) + HCl (p)	+
Alkaloids	Dragendorff	+
Terpenoids	Liebermann Burchard	+
Steroids	Liebermann Burchard	-
Tannin	FeCl ₃ (aq) 5%	+
Saponin	Aquadest HCl 2N	+

Based on Table 1, the phytochemical screening results indicate that the Goji berry (*Lycium barbarum L.*) extract tested positive for flavonoids, alkaloids, terpenoids, tannins, and saponins, as evidenced by positive (+) reactions in the respective reagent tests. In contrast, steroid compounds showed negative (-) results, indicating that the Goji berry extract does not contain steroids. These findings suggest that the major secondary metabolites present in the Goji berry extract are dominated by compounds with potential biological activities, particularly those associated with anti-inflammatory effects and wound healing.

Furthermore, an analysis of the mean neutrophil cell counts was conducted to assess the inflammatory response following tooth extraction after administration of the Goji berry (*Lycium barbarum L.*) extract. The mean neutrophil counts for each treatment group were calculated on days 1, 3, 5, and 7, representing the dynamics of the inflammatory phase during the wound

healing process. The complete results of the mean neutrophil cell counts are presented in Table 2.

Based on Table 2, the results showed that the mean neutrophil cell counts after administration of Goji berry extract at concentrations of 15%, 30%, and 55% in Wistar rats (*Rattus norvegicus*) following tooth extraction were 154.50 ± 82.731 , 158.00 ± 98.995 , and 169.00 ± 111.723 , respectively. In comparison, the positive control group (povidone iodine) and the negative control group (no treatment) showed mean neutrophil counts of 195.00 ± 103.236 and 110.00 ± 8.485 , respectively. On day 3, the mean neutrophil counts in the Goji berry extract groups at concentrations of 15%, 30%, and 55%, as well as in the positive control group (povidone iodine), decreased to 85.50 ± 0.707 , 79.00 ± 7.071 , 70.00 ± 5.657 , and 63.50 ± 2.121 , respectively, whereas the negative control group (no treatment) showed an increase to 141.50 ± 9.192 .

Table 2. Mean Neutrophil Cell Counts After Administration of Goji Berry (*Lycium barbarum L.*) Extract in Wistar Strain Rats on Days 1, 3, 5, and 7 Post-Tooth Extraction

Day	Group	$\bar{x} \pm S$
1	K-	110.00±8.485
	K+	195.00±103.236
	Goji berry extract 15%	154.50±82.731
	Goji berry extract 30%	158.00±98.995
	Goji berry extract 55%	169.00±111.723
3	K-	141.50±9.192
	K+	63.50±2.121
	Goji berry extract 15%	85.50±0.707
	Goji berry extract 30%	79.00±7.071
	Goji berry extract 55%	70.00±5.657
5	K-	109.50±24.749
	K+	54.50±0.707
	Goji berry extract 15%	69.50±2.121
	Goji berry extract 30%	63.50±0.707
	Goji berry extract 55%	56.50±2.121
7	K-	87.00
	K+	41.00±1.414
	Goji berry extract 15%	62.00±1.414
	Goji berry extract 30%	59.50±0.707
	Goji berry extract 55%	49.50±2.121

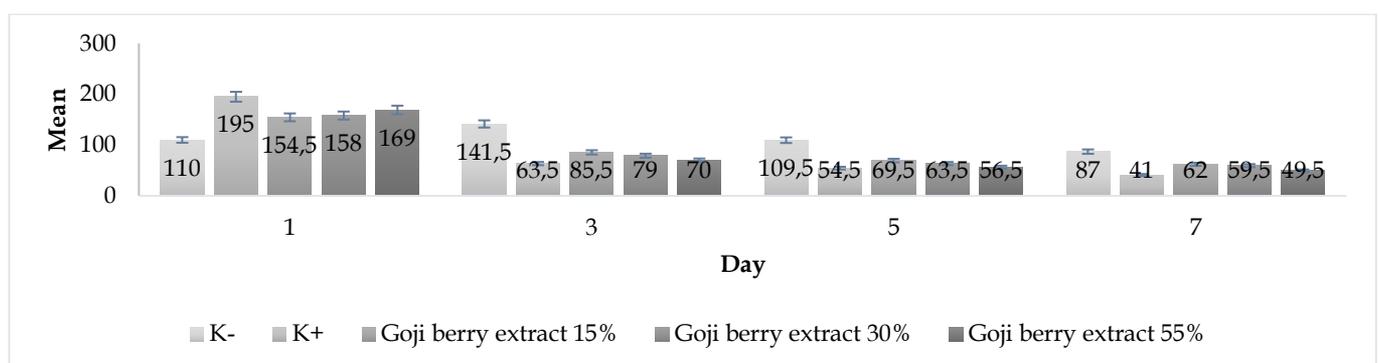


Figure 1. Average number of neutrophil cells in all groups on days 1, 3, 5, 7

As presented in Table 2, on day 5 the neutrophil cell counts in the groups treated with Goji berry extract at concentrations of 15%, 30%, and 55%, the positive control group (povidone iodine), and the negative control group (no treatment) were 69.50 ± 2.121 , 63.50 ± 0.707 , 56.50 ± 2.121 , 54.50 ± 0.707 , and 109.50 ± 24.749 , respectively. On day 7 post-tooth extraction, the lowest mean neutrophil cell count was observed in the positive control group (povidone iodine), with a mean value of 41.00 ± 1.414 , whereas the Goji berry extract groups at concentrations of 15%, 30%, and 55%, as well as the negative control group (no treatment), exhibited mean neutrophil counts of 62.00 ± 1.414 , 59.50 ± 0.707 , 49.50 ± 2.121 , and 87.00 , respectively.

Table 3. Results of Normality and Homogeneity Tests

Groups	Normality p-value	Homogeneity p-value
K-	0.179	
K+	0.260	0.060
Goji berry extract 15%	0.053	
Goji berry extract 30%	0.148	

As a preliminary step before conducting further statistical analysis, the mean neutrophil count data were

first tested for normality and homogeneity to determine the appropriate statistical test. Normality testing was performed using the Shapiro-Wilk test, while homogeneity of variance testing was performed using the Levene test. The complete results of the normality and homogeneity tests are presented in Table 3.

Based on Table 3, the Shapiro-Wilk normality test results showed that all treatment groups had p-values greater than 0.05, namely the negative control group (K-) with a p-value of 0.179, the positive control group (K+) with a p-value of 0.260, the 15% Goji berry extract group with a p-value of 0.053, and the 30% Goji berry extract group with a p-value of 0.148. These results indicate that the mean neutrophil cell count data in all groups were normally distributed. Furthermore, the homogeneity test using Levene's test yielded a p-value of 0.060 ($p > 0.05$), indicating that the variances among groups were homogeneous. Therefore, the data met the assumptions for parametric statistical analysis using one-way analysis of variance (ANOVA). The results of the one-way ANOVA examining the potential effectiveness of Goji berry (*Lycium barbarum L.*) extract on neutrophil cell counts in Wistar rats (*Rattus norvegicus*) following tooth extraction are presented in detail in Table 4.

Table 4. Potential Effectiveness of Goji Berry (*Lycium barbarum L.*) Extract on Neutrophil Cell Counts in Wistar Rats (*Rattus norvegicus*) Post-Tooth Extraction

Day	Group	$\bar{x} \pm SD$	p-value
1	K-	110.00±8.485	0.905
	K+	195.00±103.236	
	Goji berry extract 15%	154.50±82.731	
	Goji berry extract 30%	158.00±98.995	
	Goji berry extract 55%	169.00±111.723	
3	K-	141.50±9.192	0.000*
	K+	63.50±2.121	
	Goji berry extract 15%	85.50±0.707	
	Goji berry extract 30%	79.00±7.071	
	Goji berry extract 55%	70.00±5.657	
5	K-	109.50±24.749	0.021*
	K+	54.50±0.707	
	Goji berry extract 15%	69.50±2.121	
	Goji berry extract 30%	63.50±0.707	
	Goji berry extract 55%	56.50±2.121	
7	K-	87.00	0.000*
	K+	41.00±1.414	
	Goji berry extract 15%	62.00±1.414	
	Goji berry extract 30%	59.50±0.707	
	Goji berry extract 55%	49.50±2.121	

*Significant

Based on Table 4, the results of the one-way ANOVA indicated that there were significant

differences in neutrophil cell counts among all groups on days 3, 5, and 7 ($p < 0.05$), whereas no significant

difference was observed on day 1 ($p > 0.05$). Goji berry (*Lycium barbarum L.*) extract demonstrated potential in reducing neutrophil cell counts in Wistar rats (*Rattus norvegicus*) following tooth extraction on days 3, 5, and 7; however, no potential effect on neutrophil cell counts was observed on day 1. Subsequently, a post hoc Least

Significant Difference (LSD) test was performed to assess differences in the potential effectiveness of Goji berry (*Lycium barbarum L.*) extract on neutrophil cell counts between pairs of treatment groups following tooth extraction in Wistar rats (*Rattus norvegicus*). The complete results are presented in Table 5.

Table 5. Differences in the Potential Effectiveness of Goji Berry (*Lycium barbarum L.*) Extract on Neutrophil Cell Counts in Wistar Rats (*Rattus norvegicus*) Post-Tooth Extraction

Day	Group	K-	K+	Goji berry extract 15%	Goji berry extract 30%	Goji berry extract 55%
1	K-	-	0.385	0.639	0.614	0.538
	K+	-	-	0.669	0.696	0.783
	Goji berry extract 15%	-	-	-	0.970	0.877
	Goji berry extract 30%	-	-	-	-	0.907
	Goji berry extract 55%	-	-	-	-	-
3	K-	-	0.000*	0.000*	0.000*	0.000*
	K+	-	-	0.013*	0.046*	0.318
	Goji berry extract 15%	-	-	-	0.318	0.046*
	Goji berry extract 30%	-	-	-	-	0.185
	Goji berry extract 55%	-	-	-	-	-
5	K-	-	0.004*	0.016*	0.009*	0.005*
	K+	-	-	0.237	0.457	0.865
	Goji berry extract 15%	-	-	-	0.614	0.297
	Goji berry extract 30%	-	-	-	-	0.558
	Goji berry extract 55%	-	-	-	-	-
7	K-	-	0.000*	0.000*	0.000*	0.000*
	K+	-	-	0.000*	0.000*	0.001*
	Goji berry extract 15%	-	-	-	0.121	0.000*
	Goji berry extract 30%	-	-	-	-	0.001*
	Goji berry extract 55%	-	-	-	-	-

*Significant

Based on Table 5, on day 1, the results showed no significant differences in the potential effectiveness on neutrophil cell counts between the Goji berry extract groups at concentrations of 15%, 30%, and 55% and the positive control group (povidone iodine). Similarly, on day 1, there were no significant differences in potential effectiveness between all concentrations of Goji berry extract and the negative control group (no treatment) ($p > 0.05$).

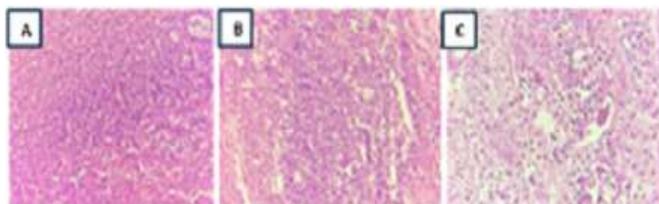


Figure 2. Histopathological images on day 1

On day 3, the post hoc LSD test revealed significant differences in the potential effectiveness on neutrophil cell counts between the 15% and 30% Goji berry extract groups and the positive control group (povidone iodine), as well as between the 15%, 30%, and 55% Goji berry extract groups and the negative control group (no

treatment) ($p < 0.05$). No significant difference in potential effectiveness was observed between the positive control group (povidone iodine) and the 55% Goji berry extract group ($p > 0.05$).

On day 5, the post hoc LSD results indicated that there were significant differences in the potential effectiveness on neutrophil cell counts between all concentrations of Goji berry extract and the negative control group (no treatment) ($p < 0.05$). In contrast, comparisons between the positive control group (povidone iodine) and the 15%, 30%, and 55% Goji berry extract groups showed no significant differences in neutrophil cell counts in Wistar rats (*Rattus norvegicus*) post-tooth extraction ($p > 0.05$).

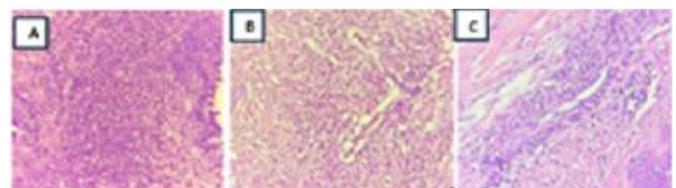


Figure 3. Histopathological images on day 5

The post hoc LSD test results on day 7 post-tooth extraction indicated that there were significant

differences in the potential effectiveness on neutrophil cell counts in Wistar rats (*Rattus norvegicus*) between the 15%, 30%, and 55% Goji berry extract groups and both the positive control group (povidone iodine) and the negative control group (no treatment) ($p < 0.05$).

Discussion

Goji berry (*Lycium barbarum L.*) has been reported to possess beneficial health properties (Putri et al., 2020). Based on the plant identification conducted at the Herbarium Medanense, Universitas Sumatera Utara, it can be confirmed that the goji berry fruits used in this study were derived from the species *Lycium barbarum L.*

Goji berry fruits have been used as anti-inflammatory and antipyretic agents in traditional Chinese medicine (Ávila et al., 2020). In addition, Goji berry has been shown to prevent free radicals, enhance the antioxidant mechanism of GSH, protect DNA from inflammation, reduce lipid peroxidation, and decrease protein oxidation in muscle cells (Putri et al., 2020; Skenderidis et al., 2022). The health benefits of Goji berry fruits are likely attributed to their secondary metabolite content. Phytochemical screening is an initial step that provides a general overview of the secondary metabolites present in natural materials under study. Qualitatively, this method can be conducted through colorimetric reactions using specific reagents (Emilia et al., 2023). The results presented in Table 1 indicate that the Goji berry extract tested positive for flavonoids, alkaloids, terpenoids, tannins, and saponins.

The flavonoid compounds contained in Goji berry (*Lycium barbarum L.*) exert anti-inflammatory effects by inhibiting cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, resulting in a reduction in the number of inflammatory cells (Jomova et al., 2025; Ysrafil et al., 2023). Flavonoids in Goji berry inhibit the formation of inflammatory mediator enzymes such as phospholipase A2 (PLA2), LOX, and COX, thereby reducing the production of leukotrienes (LT) and prostaglandins (PG), which produce an antagonistic effect against inflammation (Ysrafil et al., 2023). In addition to flavonoids, alkaloids also play a role during the inflammatory phase by limiting inflammation through the reduction of histamine and prostaglandin release, which are inflammatory mediators, and by preventing excessive entry of free radicals (Anggayanti et al., 2024; Jomova et al., 2025).

Tannins can enhance vascularization and have the ability to induce Transforming Growth Factor- β (TGF- β), a homodimeric protein produced by various cell types, including platelets, neutrophils, endothelial cells, lymphocytes, and macrophages. TGF- β plays a role in stimulating cell migration (Barboura et al., 2022; Prabhath et al., 2024). As an anti-inflammatory agent, the

active saponin compounds inhibit exudate formation and reduce vascular permeability (Prehananto et al., 2023).

Tooth extraction can cause tissue injury and trigger a healing process involving both soft tissue and the alveolar bone (Azizah et al., 2024). When injury occurs, neutrophils are the first white blood cells to appear and initiate inflammation. An increased number of neutrophils at the wound site indicates the presence of ongoing inflammation (Margraf et al., 2022; Yang et al., 2025). This study was conducted on 30 male Wistar rats (*Rattus norvegicus*) to evaluate the potential effectiveness of Goji berry (*Lycium barbarum L.*) extract on neutrophil cell counts following tooth extraction, with observations conducted at four time points: days 1, 3, 5, and 7. Wound healing was monitored on days 1, 3, 5, and 7 to track the transition from the inflammatory phase to the proliferative phase. Specifically, day 1 represented hemostasis and neutrophil infiltration, day 3 marked the peak of inflammation with macrophage dominance, day 5 showed a reduction in inflammatory cells along with the onset of fibroblast activity and angiogenesis, and day 7 represented the peak of proliferation with granulation tissue formation (Purnama et al., 2017).

Based on the study results, the highest neutrophil cell counts were observed on day 1, followed by a decrease on days 3, 5, and 7 in the Goji berry extract and povidone iodine groups, whereas the negative control group showed an increase on day 3 and a subsequent decrease on days 5 and 7. According to Anggayanti et al. (2024), the treatment and positive control groups began to show a reduction in neutrophil counts during the inflammatory phase post-tooth extraction in Wistar rats on day 3, while the negative control group showed a decrease on day 5. Similarly, in the study by Azizah et al. (2024) the peak mean neutrophil count occurred on day 3, followed by a decline from day 5 to day 7.

The findings of this study are consistent with the statements of Soesilawati et al., cited in Azizah et al. (2024) which report that neutrophil counts increase rapidly during the first 12 hours after injury, reaching a peak on days 1 to 2, remaining relatively stable until day 3, and then decreasing sharply by day 5. During this period, hemostasis and phagocytosis occur. Following wound formation, vasoconstriction leads to blood clotting, covering the wound area. The subsequent phase involves vasodilation, which increases blood flow and facilitates neutrophil migration to the wound site to eliminate bacteria (Borges et al., 2024). A significant decrease in neutrophil counts was observed in all groups on days 5 and 7. This condition indicates that by day 5, the wound healing process has progressed beyond the late inflammatory phase and has begun entering the proliferative phase. During the transition from the

inflammatory to the proliferative phase, neutrophils undergo apoptosis and are subsequently cleared by macrophages, signaling the resolution of the inflammatory process (Azizah et al., 2024).

Neutrophils are the first cells to appear in large numbers during the early stage of inflammation, acting as the body's primary defense against foreign invasion and digesting bacteria and dead cells (Uribe-querol & Rosales, 2024). They produce pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6, thereby enhancing the inflammatory response. Neutrophils at the wound site serve as inflammatory mediators to combat infection. However, if they remain in the wound, they can cause cellular damage, delay wound healing, and potentially lead to chronic wounds (Gao et al., 2024; Yang et al., 2025). On day 3, administration of Goji berry (*Lycium barbarum L.*) extract resulted in a reduction in neutrophil counts. This reduction may accelerate the healing process, indicating that wound repair is progressing to the next stage (Hervina et al., 2024).

The results of the one-way ANOVA indicated that there were significant differences in neutrophil cell counts among all groups on days 3, 5, and 7 ($p < 0.05$), whereas no significant difference was observed on day 1 ($p > 0.05$). Goji berry (*Lycium barbarum L.*) extract demonstrated anti-inflammatory potential by reducing neutrophil counts in Wistar rats (*Rattus norvegicus*) following tooth extraction. These findings are consistent with the study by Ávila et al. (2020) which reported that administration of Goji berry extract showed potential in reducing the inflammatory response. Similarly, Azizah et al. (2024) observed significant differences in neutrophil counts among all treatment and control groups on days 3, 5, and 7.

Povidone iodine was chosen as the positive control due to its well-established ability to accelerate wound healing, with anti-inflammatory and antimicrobial properties as well as the capacity to stimulate angiogenesis (Harun et al., 2024). Based on the post hoc LSD test results, the differences between the positive control and treatment groups were not highly significant on days 1 and 3, whereas the negative control showed significantly higher mean neutrophil counts. This indicates that the inflammatory process decreased following the administration of povidone iodine and Goji berry. These findings differ from those reported by Azizah et al. (2024) who noted significant differences between povidone iodine and the treatment groups on days 3, 5, and 7, with the treatment groups exhibiting the lowest neutrophil counts throughout the observation period.

The decrease in neutrophils on day 3 in the Goji berry and povidone iodine groups is suspected to be due to apoptosis, reflecting their role as phagocytic agents.

These cells are subsequently replaced by fibroblasts, which regenerate tissue and form new tissue (Riyani et al., 2021). Furthermore, the reduction in inflammatory cells, including lymphocytes, neutrophils, and macrophages, indicates that the healing process has progressed to the next stage, thereby accelerating both the inflammatory response and wound healing (Cao et al., 2023).

Conclusion

Based on the study results, it can be concluded that Goji Berry extract (*Lycium barbarum L.*) at concentrations of 15%, 30%, and 55% demonstrates significant potential effectiveness in reducing neutrophil cell counts in Wistar rats (*Rattus norvegicus*) following tooth extraction, with the 55% concentration showing the most optimal effectiveness. These findings indicate that Goji Berry extract may play a role in controlling the inflammatory response during the early phase of post-tooth extraction wound healing. In this regard, further studies are recommended, including toxicity testing to ensure the safety of Goji Berry extract at various concentrations, clinical trials involving post-tooth extraction patients to directly evaluate its effectiveness and safety in humans, and the development of Goji Berry extract as an alternative herbal therapy to accelerate wound healing after tooth extraction.

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Author Contributions

Conceptualization, S.L. and T.A.S.P.; methodology, S.L.; validation, S.L. and T.A.S.P.; formal analysis, S.L.; investigation, S.L.; resources, S.L.; data curation, S.L.; writing—original draft preparation, S.L.; writing—review and editing, S.L. and T.A.S.P.; visualization, S.L.; supervision, T.A.S.P.; project administration, T.A.S.P.; funding acquisition, T.A.S.P.

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Conflicts of Interest

No conflict of interest.

References

Anggayanti, N. A., Dewi, I. A. N. N., & Dewi, D. A. D. N. (2024). Efektivitas Gel Ekstrak *Ocimum basilicum L.* 15 % terhadap jumlah sel neutrofil pada fase inflamasi pasca Ekstraksi gigi tikus wistar: Studi neutrophil cell count in the inflammatory phase after tooth. *Jurnal Kedokteran*

- Gigi Universitas Padjadjaran*, 36(3), 371–379. <https://doi.org/10.24198/jkg.v36i3.58977>
- Ávila, C. N., Trindade, F. M. R., Penteado, J. O., & Janke, F. (2020). Anti-inflammatory Effect of a Goji Berry Extract (*Lycium barbarum*) in Rats Subjected to Inflammation by Lipopolysaccharides (LPS). *Brazilian Archives of Biology and Technology*, 63, 1–11. <https://dx.doi.org/10.1590/1678-4324-2020180612>
- Azizah, K. U., Anwaristi, A. Y., Kurniawati, D., & Ningsih, J. R. (2024). Efektivitas Gel Ekstrak Daun Binahong (*Anredera cordifolia*) 5% Terhadap Jumlah Neutrofil pada Proses Penyembuhan Luka Pasca Pencabutan Gigi Tikus strain Wistar. *ARTERI: Jurnal Ilmu Kesehatan*, 5(3), 1–8. <https://doi.org/10.37148/arteri.v5i3.434>
- Barboura, M., Cornebise, C., Hermetet, F., Guerrache, A., Selmi, M., Salek, A., Chekir-ghedira, L., Aires, V., & Delmas, D. (2022). Tannic Acid, A Hydrolysable Tannin, Prevents Transforming Growth Factor- β -Induced Epithelial–Mesenchymal Transition to Counteract Colorectal Tumor Growth. *Cells*, 11(3645), 1–19. <https://doi.org/10.3390/cells11223645>
- Borges, A., Vaz, J. A., & Calhelha, R. C. (2024). Enhancing Wound Healing: A Comprehensive Review of Sericin and Chelidonium majus L. as Potential Dressings. *Materials*, 17(4199), 1–43. <https://doi.org/10.3390/ma17174199>
- Cao, L., Ma, L., Zhao, J., Wang, X., Fang, X., & Li, W. (2023). An Unexpected Role of Neutrophils in Clearing Apoptotic Hepatocytes in Vivo. *ELife*, 20(12), 1–26. <https://doi.org/10.7554/eLife.86591>
- Cui, C., Zhao, D., Huang, J., & Hao, J. (2022). Progress on research and development of goji berry drying: A review. *International Journal of Food Properties*, 25(1), 435–449. <https://doi.org/10.1080/10942912.2022.2046054>
- Djuma, E., & Kurnia, D. A. (2024). Efektivitas penggunaan terapi topical herbal pada perawatan ulkus kaki diabetik: A systematic literature review. *Holistik Jurnal Kesehatan*, 18(2), 202–208. <https://doi.org/10.33024/hjk.v18i2.281>
- Emilia, I., Setiawan, A. A., Novianti, D., Rangga, & Mutiara, D. (2023). Skrining Fitokimia Ekstrak Daun Sugkai (*Peronema canescens* Jack.) secara Infundasi dan Maserasi. *Jurnal Indobiosains*, 5(2), 95–102. <https://doi.org/10.31851/indobiosains.v5i2.12597>
- Gao, M., Guo, H., Dong, X., Wang, Z., & Yang, Z. (2024). Regulation of Inflammation During Wound Healing: the Function of Mesenchymal Stem Cells and Strategies for Therapeutic Enhancement. *Frontiers in Pharmacology*, 15(February), 1–15. <https://doi.org/10.3389/fphar.2024.1345779>
- Halim, S., Halim, H., Lister, I. N. E., Sihotang, S., Nasution, A. N., & Girsang, E. (2021). Efektivitas gel ekstrak etanol daun senggani (*Melastoma candidum* D. Don.) terhadap diameter luka pasca pencabutan gigi pada tikus putih (*Rattus norvegicus*). *Bioma: Jurnal Ilmiah Biologi*, 10(1), 44–54. <https://doi.org/10.26877/bioma.v10i1.6555>
- Harun, H., Haroen, H., Mirwanti, R., Apriani, N., & Akuoko, C. P. (2024). Uncovering the Benefits of Povidone Iodine Compared to Other Therapeutic Agents in Wound Infection Prevention and Healing Outcomes: A Scoping Review. *Journal of Multidisciplinary Healthcare*, 17(July), 3605–3616. <https://doi.org/10.2147/JMDH.S469037>
- Hervina, H., Haryani, I. G. A. D., & Aryandana, N. M. D. P. (2024). Pemberian Vitamin D Menyebabkan Jumlah Sel Neutrofil Lebih Rendah Dibanding Kontrol pada Tikus Wistar yang Diinduksi Periodontitis. *Bali Dental Science and Exhibition (Bali Dence)*, 28, 260–272. Retrieved from <https://e-journal.unmas.ac.id/index.php/BDSE/article/view/10747>
- Istiqomah, I. N., Mashuri, Abdillah, A., & Azizah, L. N. (2024). Potensi Tanaman Ganjan (*Artemisia vulgaris*) dalam Penyembuhan Luka Sayat pada Tikus (Sprague Dawley). *Jurnal Tumbuhan Obat Indonesia*, 17(1), 56–65. <https://doi.org/10.31002/jtoi.v16i2.885>
- Jomova, K., Alomar, S. Y., Valko, R., Liska, J., Nepovimova, E., Kuca, K., Valko, M., & Valko, M. (2025). Chemico-Biological Interactions Flavonoids and their Role in Oxidative Stress, Inflammation, and Human Diseases. *Chemico-Biological Interactions*, 413(February), 1–44. <https://doi.org/10.1016/j.cbi.2025.111489>
- Margraf, A., Lowell, C. A., & Zarbock, A. (2022). Neutrophils in Acute Inflammation: Current Concepts and Translational Implications. *Blood*, 139(14), 2130–2144. <https://doi.org/10.1182/blood.2021012295>
- Oki, A. S., & Amalia, N. (2020). Wound healing acceleration in inflammation phase of post-tooth extraction after aerobic and anaerobic exercise. *Science & Sports*, 35(3), 168–e1. <https://doi.org/10.1016/j.scispo.2019.06.001>
- Prabhath, S., Bhat, K. M. R., Pai, K. S. R., Kinra, M., & Gourishetti, K. (2024). A Biochemical and Molecular Insight to Wound Healing Properties of Traditional Indian Medicines in Normal and Diabetic Rats. *Ind. J. Pharm. Edu. Res*, 58(2), 359–371. <https://doi.org/10.5530/ijper.58.2s.39>
- Prehananto, H., Purnamasari, V. D., & Yuliasri, N.

- (2023). Uji Aktivitas Ekstrak Daun Kemangi dalam Meningkatkan Jumlah Fibroblas pada Traumatik Ulser. *Bhakta Dental Jurnal*, 1(1), 1–8. Retrieved from <https://bdj.iik.ac.id/index.php/bdj/article/view/11>
- Prestiyanti, N. M. I., Adiatmika, I. P. G., & Muliarta, I. M. (2021). Pemberian pasta ekstrak daun pegagan 10% lebih meningkatkan jumlah sel fibroblas dan reepitelisasi pada soket mandibula daripada pasta ekstrak daun mengkudu 10% pasca pencabutan gigi marmut jantan. *Intisari Sains Medis*, 12(3), 718–723. <https://doi.org/10.15562/ism.v12i3.1114>
- Purnama, H., Sriwidodo, & Ratnawulan, S. (2017). Review Sistematis: Proses Penyembuhan Dan Perawatan Luka. *Farmaka*, 15(2), 251–258. <https://doi.org/10.24198/jf.v15i2.13366>
- Putri, E. B. P., Putri, F. K., & Sulaiha, S. (2020). Perbandingan Kadar Flavonoid dan Vitamin C pada Infused Water Goji Berry (*Lycium barbarum*) dan Air Nabeez Kurma (*Phoenix dactylifera L.*). *MTPH*, 4(1), 32–37. <https://doi.org/10.33086/mtphj.v4i1.1458>
- Rahmawati, A. A., Harijadi, A., Kristanto, Y., & Asmarani, Y. K. (2023). Pengaruh Gel Ekstrak Bawang Merah terhadap Jumlah Fibroblas pada Luka Ekstraksi Gigi Tikus Jantan Wistar. *Bhakta Dental Journal*, 1(2), 1–7. <https://doi.org/10.56710/bhaktadent.v1i2.17>
- Riyani, N. J., Pasaribu, R., Mardiyantoro, K. F., & Gigi, F. K. (2021). Evaluasi Jumlah Limfosit Pasca Aplikasi Lendir Bekicot (*Achatina fulica*) pada Soket Tikus Wistar (*Rattus norvegicus*). *Sinnun Maxillofacial Journal*, 3(1), 42–49. <https://doi.org/10.33096/smj.v3i01.31>
- Skenderidis, P., Leontopoulos, S., & Lampakis, D. (2022). Goji Berry: Health Promoting Properties. *Nutraceuticals*, 2(1), 32–48. <https://doi.org/10.3390/nutraceuticals2010003>
- Uribe-querol, E., & Rosales, C. (2024). Neutrophils versus Protozoan Parasites: Plasmodium . *Microorganisms*, 12(827), 1–32. <https://doi.org/10.3390/microorganisms12040827>
- Yang, L., Shi, F., & Wang, L. (2025). Neutrophils in Tissue Injury and Repair: Molecular Mechanisms and Therapeutic Targets. *MedComm*, 6(e70184), 1–18. <https://doi.org/10.1002/mco2.70184>
- Ysrafil, Y., Sapiun, Z., Slamet, N. S., Mohamad, F., Hartati, H., Damiti, S. A., Alexandra, F. D., Rahman, S., Masyeni, S., Harapan, H., & Mamada, S. S. (2023). Anti-inflammatory Activities of Flavonoid Derivates. *ADMET & DMPK*, 11(3), 331–359. <https://doi.org/10.5599/admet.1918>