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Original Article

Topical noni leaf extract cream enhances platelet-derived growth factor and reduces TNF-α in incision wound healing: an in vivo study

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A B S T R A C T

Background: Noni (*Morinda citrifolia L.*) leaves contain flavonoids, tannins, and saponins with antioxidant and anti-inflammatory effects. Although studies demonstrate their potential in wound healing, evidence on topical noni leaf extract cream and its effect on TNF-α and platelet-derived growth factor (PDGF) in incision wounds remains limited.

Objective: This study aimed to assess the effects of noni leaf extract cream on TNF-α and PDGF levels in Wistar rats with incised wounds.

Method: A post-test only controlled laboratory experiment was conducted using five groups: healthy rats (KS), untreated incision wounds (KN), povidone-iodine (KP), 20% noni extract cream (P1), and 40% noni extract cream (P2). Treatments were applied for 3 days. TNF-α and PDGF levels were measured using ELISA. Data were analyzed using one-way ANOVA followed by LSD post-hoc test.

Results: TNF-α levels differed significantly between groups (p=0.000), with the highest value in the KN group (220.68±47.16 pg/mL) and the lowest in KP (76.59±20.74 pg/mL). Both P1 and P2 showed decreased TNF-α compared to KN. PDGF levels differed significantly (p=0.000), with the lowest in KN (54.42±7.51 pg/mL) and the highest in P2 (364.34±33.96 pg/mL).

Conclusion: Noni leaf extract cream at 20% and 40% effectively reduced TNF-α and increased PDGF levels, indicating enhanced inflammatory resolution and proliferative activity in incision wound healing.

INTRODUCTION

Wound healing is a coordinated biological process that occurs when tissue is damaged restore its structural and functional integrity through the phases of inflammation, proliferation, and remodeling.[1,2] This process requires balanced molecular regulation disruption of inflammatory control can delay healing and increase the risk of excessive scar formation.[3] An incised wound is defined as a sharp-edged injury caused by a cutting object and is commonly encountered in surgical procedures. This type of wound involves damage to the epidermis and dermis and depends heavily on inflammatory mediators such as TNF-α and platelet-derived growth factor (PDGF) to achieve optimal healing.[4] TNF-α plays a critical role during the early inflammatory response, whereas PDGF supports fibroblast proliferation and new tissue formation.[5,6]

Dysregulation of these mediators can lead to delayed healing, prolonged inflammation, or the development of hypertrophic scars.[7] Globally, post-injury scar complications are reported in 40–70% of cases. In Indonesia, postoperative wound complications are estimated at 10–20%, contributing to the growing need for effective and safe topical therapies. This situation underscores interest in natural compounds as wound-healing agents.[8]

Noni *(Morinda citrifolia L.)* leaves contain bioactive compounds flavonoids, tannins, saponins, and alkaloids known for their anti-inflammatory, antioxidant, and antibacterial properties.[9] These compounds may reduce inflammation, modulate oxidative stress, and enhance tissue regeneration.[10] Several studies have reported that noni leaf extract accelerates wound contraction and increases fibroblast activity. However, several research gaps remain. First, most previous studies evaluated wound healing only macroscopically without assessing molecular biomarkers such as TNF-α and PDGF.[11,12] Second, many studies used excision wound models, which do not fully represent incised wounds commonly encountered in clinical settings.[13-14] Third, topical formulations tested previously generally contained low extract concentrations and lacked evaluation in clinically relevant cream preparations.

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Therefore, the novelty of this study lies in the use of high-concentration noni leaf extract creams (20% and 40%) applied to a standardized incised wound model, combined with molecular analysis of TNF-α and PDGF using ELISA to provide a more comprehensive understanding of wound-healing mechanisms. Based on these considerations, this study aimed to determine the effects of noni leaf extract cream on TNF-α and PDGF levels in Wistar rats with incised wounds and to compare the effectiveness of 20% and 40% formulations in supporting the wound-healing process.

METHOD

Study Design

This study is a laboratory experimental study with a post-test only control group design.[10]

Study Site

The research was conducted at *Stem Cell and Cancer Research* SCCR) Semarang, for a period of 6-8 weeks in October-November 2024 from preparation to data analysis.

Materials

The study utilized standard surgical instruments, basic laboratory equipment, and ELISA assay tools. The materials included adult Wistar rats, noni *(Morinda citrifolia L.*) leaf extract, phosphate-buffered saline (PBS), formalin, and xylazine–ketamine anesthesia.

Experimental Procedure

The study consisted of five groups: healthy rats without incisions (KS), rats with incised wounds without treatment (KN), rats treated with povidone-iodine cream (KP), rats treated with 20% noni leaf extract cream (P1), and rats treated with 40% noni leaf extract cream (P2), each receiving treatment for three days.

Preparation Before Treatment

Thirty white Wistar rats were prepared in the SCCR Laboratory. In the treatment group, the incised wound area of the rats was given noni leaf extract, while in the control group no treatment/placebo/buffer solution/standard treatment was given. Then the rats were adapted for 7 days in the prepared environment, and given food and water.

Making Noni Leaf Extract Cream

The noni leaf extract used in this study was obtained from the extraction process of noni leaves obtained from the Pedurungan area of Semarang City, then using 70% ethanol solvent with the stages of making simplicia, maceration and evaporation. The extract was subsequently formulated into cream preparations with a concentration of 20% and 40% and tested for flavonoid levels, the cream was applied topically 1x/day to the cut wound as much as 0.2gr for 3 days.

Rat Termination

The incision was made on the back skin area of mice that had previously been anesthetized. A standardized incision measuring 1 cm × 2 mm was created using a sterile scalpel. Noni leaf extract cream was given to the treatment group in the incision area for 3 days.

Skin Biopsy Preparation

Skin tissue from the incision area was collected on day 4 from all groups for biomarker analysis after treatment administration of noni extract, then he collected skin samples were subsequently analyzed to determine the levels of TNF-α and PDGF levels using the ELISA method

Observation of Results

The skin tissue samples that had been obtained were then analyzed for TNF-α and PDGF levels using the ELISA method, following the procedure attached to the product, using a microplater reader with a wavelength of 450nm.

Data Analysis

The TNF-α and PDGF data met the assumptions of normality and homogeneity, allowing analysis using one-way ANOVA. Significant group differences were then further examined with an LSD post-hoc test to compare the effects of the noni leaf extract cream on TNF-α and PDGF levels.

Ethical Considerations

This research has obtained ethical approval from the Faculty of Medicine, Sultan Agung Islamic University, Semarang with the number 392/X/2024/Bioethics Commission.

RESULTS

Phytochemical screening confirmed the presence of key bioactive compounds in noni leaf extract. Macroscopic observations (Figure 1) showed better wound closure in the 20% and 40% cream groups, with the 40% cream producing the most notable improvement. As presented in Table 1, TNF-α levels were significantly lower in all treated groups compared to the untreated group, while PDGF levels increased markedly ($p<0.001$), indicating improved inflammatory regulation and enhanced proliferative activity. The untreated group exhibited the highest TNF-α levels, confirming significant group differences (ANOVA $p<0.001$; Figure 2).

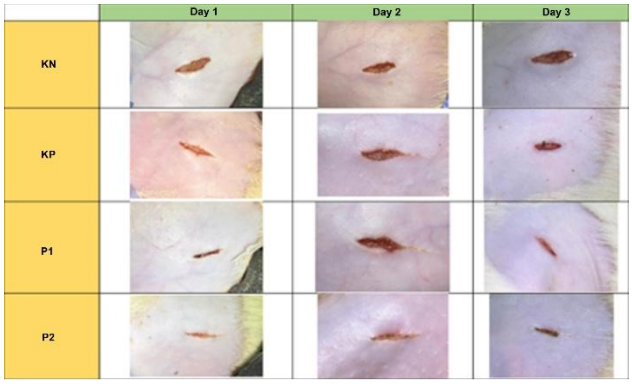

Figure 1. Macroscopic condition of incision wounds across treatment groups on days 1–3.

On day 3, PDGF levels varied across groups: KS 156.02 pg/mL, KN 54.42 pg/mL, KP 106.24 pg/mL, P1 354.26 pg/mL, and P2 364.34 pg/mL. The negative control group showed the lowest PDGF level, while the 40% noni leaf extract cream (P2) produced the highest increase (Table 2). Overall, P2 demonstrated the most substantial rise in PDGF levels, as shown in Figure 3.

Table 1. TNF-α Levels in Each Treatment Group

Group	Treatment Description	TNF-α (pg/dL) Mean ± SD
KS	Healthy mice	67.45 ± 16.21
KN	No intervention	220.68 ± 47.16
KP	Povidone-iodine	76.59 ± 20.74
P1	Noni extract cream 20%	99.53 ± 11.65
P2	Noni extract cream 40%	85.61 ± 17.50

Exp: *Shapiro–Wilk* (p>0.05), *Levene's test* (p=0.190*), One-Way Anova* (p=0.000)

Table 2. PDGF Levels in Each Treatment Group

Group	Treatment Description	PDGF (ng/dL) Mean ± SD
KS	Healthy mice	156.02 ± 31.97
KN	No intervention	54.42 ± 7.51
KP	Povidone-iodine	106.24 ± 42.69
P1	Noni extract cream 20%	354.26 ± 85.82
P2	Noni extract cream 40%	364.34 ± 33.96

Exp: *Shapiro–Wilk* (p>0.05), *Levene's test* (p=0.113*), One-Way Anova* (p=0.000)

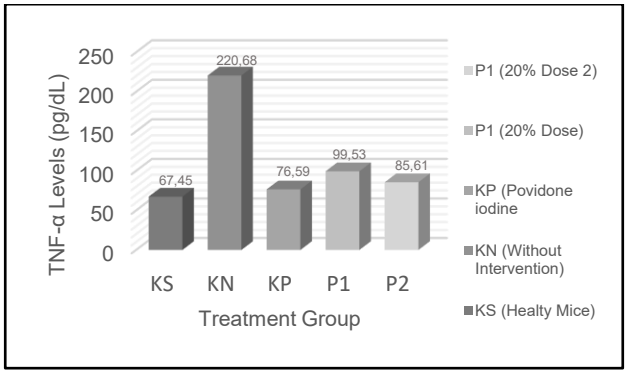

Figure 2. Mean TNF-α Levels in Each Treatment Group

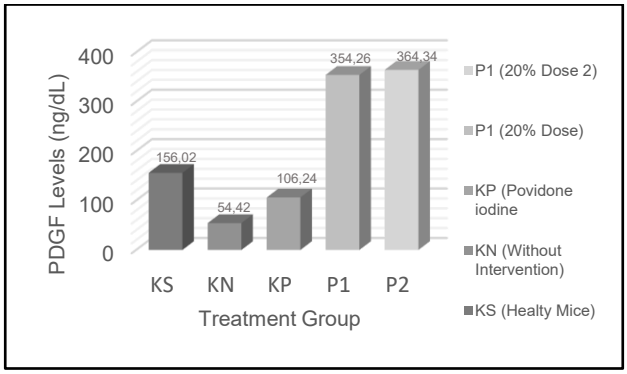

Figure 3. Average PDGF levels between groups of mice with incision wounds given noni leaf cream

DISCUSSION

This study showed that noni leaf extract cream effectively lowered TNF-α and elevated PDGF levels in Wistar rats with incision wounds. These findings suggest that the extract modulates both the inflammatory and proliferative phases of wound healing. TNF-α is a key cytokine released early during inflammation and is responsible for initiating immune cell recruitment. Excessive or prolonged TNF-α expression delays wound healing and increases tissue damage. The significant reduction of TNF-α in the treatment groups indicates that noni leaf extract suppressed excessive inflammation and promoted a more favorable healing environment.[15]

This effect is biologically plausible given noni leaves contain bioactive flavonoids, tannins, saponins, and alkaloids with established anti-inflammatory properties.[16-17] The significant increase in PDGF levels, especially in the 40% extract group, suggests enhanced proliferative activity. PDGF is critical for fibroblast proliferation and migration, angiogenesis, and extracellular matrix formation. The elevation of PDGF on day 4 aligns with the expected onset of the proliferative phase, which occurs approximately between days 3 and 14. This finding indicates that noni leaf extract may facilitate a faster transition from inflammation to tissue regeneration.[18]

The results of this study are supported by previous evidence showing that topical noni extract promotes fibroblast proliferation and accelerates wound closure. Noni leaf extract is known to increase the activity of Additional research has reported that ethanol-based noni extract suppresses TNF-α expression and reduces inflammatory cell infiltration more effectively than certain standard anti-inflammatory agents.[19] Noni extract has also been shown to support angiogenesis through increased formation of new blood vessels, which is essential for delivering oxygen and nutrients to healing tissue. Collectively, these studies corroborate the present findings.[20] No contradictory evidence was identified in the existing literature, although differences in extract concentration, wound models, or formulation type may account for variations in other studies. The molecular changes observed lower TNF-α and higher PDGF provide new insights into the biological mechanisms underlying the wound-healing potential of noni leaf extract cream.[21-23]

This study, however, has several limitations. Macroscopic wound assessment was not quantified using digital measurement, limiting the objectivity of wound size comparisons.[24] The observation period was brief, ending on day 4, which prevented evaluation of later healing phases such as collagen remodeling and scar formation. In addition, wound images represented only selected animals rather than all subjects.[25-26] Overall, the findings indicate that noni leaf extract cream, particularly at higher concentrations, can modulate early inflammation and enhance proliferative signaling, suggesting its potential as a natural topical agent for incision wound healing.

CONCLUSIONS AND RECOMMENDATION

This study demonstrated that noni leaf extract cream significantly reduced TNF-α levels and increased PDGF levels in Wistar rats with incised wounds, with both the 20% and 40% formulations showing superior effects compared with the untreated control. These findings indicate that noni leaf extract cream may support early wound healing through improved inflammatory regulation and enhanced proliferative activity. Further research with longer observation periods, objective wound-closure measurements, and clinical trials in humans is recommended to validate its safety, effectiveness, and potential for clinical application.

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