The Effect of NLRP3 Inflammasome on Wound Healing

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Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, and remodeling. One of the key regulators of the inflammatory phase is the NLRP3 inflammasome, a multiprotein complex that plays a role in the activation of caspase-1 and the release of the proinflammatory cytokine interleukin-1.β(IL-1β) and interleukin-18 (IL-18), as well as the induction of pyroptosis. Physiological activation of NLRP3 is required to initiate an immune response, but excessive activation can prolong inflammation and inhibit the wound healing process. Therefore, studying the effect of the NLRP3 inflammasome on wound healing is important as a basis for developing inflammation-modulating therapies. This study used a literature review method by examining 25 scientific articles published in 2022–2026. The literature search was conducted through the PubMed, Google Scholar, ScienceDirect, SpringerLink, Frontiers, Nature Publishing Group, and MDPI databases using keywords related to NLRP3 inflammasome, wound healing, pyroptosis, diabetic wound, and inflammation. Data were analyzed descriptively narratively to identify the mechanism of NLRP3 activation, its role in wound healing, and potential therapies targeting this pathway. The results of the synthesis indicate that the NLRP3 inflammasome plays a crucial role in regulating the inflammatory response during wound healing. Inflammasome activation is required in the early phase for pathogen elimination and clearance of damaged tissue, but excessive activation increases IL-1 production.β, IL-18, and pyroptosis, thereby inhibiting angiogenesis, fibroblast proliferation, collagen deposition, and re-epithelialization. Various studies have shown that modulating NLRP3 using probiotics, natural compounds, hydrogels, stem cell-derived extracellular vesicles, and exosomes can suppress inflammation, enhance tissue regeneration, and accelerate wound healing, especially in diabetic wounds, burns, and radiation injuries. The NLRP3 inflammasome has a dual role in wound healing: it acts as a key regulator of the inflammatory response and as a factor that can inhibit tissue regeneration if overactivated. Modulating NLRP3 activity is a promising therapeutic strategy to accelerate wound healing by controlling inflammation and enhancing tissue regeneration..

Keywords:NLRP3 inflammasome, wound healing

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1. Introduction

Wound healing is a complex and coordinated biological process, involving the interaction of various cell types, inflammatory mediators, growth factors, and extracellular matrix components to restore the integrity of damaged tissue. Physiologically, the wound healing process occurs through four main phases: hemostasis, inflammation, proliferation, and remodeling. These four phases are interrelated and must occur in balance for optimal wound healing. Disruption of any phase, particularly the inflammatory phase, can lead to delayed wound healing, excessive scar tissue formation, and even the development of chronic wounds that are difficult to treat [1].

Inflammation is a crucial initial response in the wound healing process because it eliminates microorganisms, clears necrotic tissue, and initiates tissue regeneration. However, excessive or prolonged inflammation can cause more extensive tissue damage and inhibit the healing process [2]. Therefore,

regulation of inflammatory mediators is a key factor in determining the success of the wound healing process [3].

One of the main regulators in the inflammatory response is the NLRP3 (NOD-like receptor family pyrin domain-containing 3) inflammasome, a multiprotein complex that is part of the innate immune system. NLRP3 inflammasome activation is triggered by various danger signals, such as microbial infection, oxidative stress, tissue damage, crystals, and metabolic changes [4]. Once activated, NLRP3 forms a complex with the adaptor ASC (apoptosis-associated speck-like protein containing a CARD) and procaspase-1, resulting in the production of active caspase-1 [5]. Caspase-1 activation then triggers the maturation of the proinflammatory cytokine interleukin-1.β(IL-1β) and interleukin-18 (IL-18), and induces pyroptosis, a form of inflammatory cell death that plays a role in eliminating pathogens while strengthening the inflammatory response [6].

In recent years, research on the NLRP3 inflammasome has grown rapidly due to its known role in various inflammatory diseases, including diabetes mellitus, autoimmune diseases, neurodegenerative diseases, organ fibrosis, cancer, and impaired wound healing [7]. Various studies have shown that NLRP3 activation is required in the early phase of wound healing to recruit neutrophils and macrophages to the site of injury so that the tissue clearance process can take place properly [8]. However, continuous inflammasome activation leads to increased production of IL-1β, IL-18, and other inflammatory mediators that prolong the inflammatory phase, inhibit fibroblast proliferation, reduce angiogenesis, inhibit collagen deposition, and slow re-epithelialization. These conditions are often found in chronic wounds, especially diabetic wounds, burns, and radiation wounds [9].

Several experimental studies have also shown that modulating NLRP3 inflammasome activity can enhance wound healing. Various therapeutic agents, such as Lactobacillus plantarum, ferulic acid, astaxanthin, ferulic acid-based hydrogels, stem cell-derived extracellular vesicles, and miRNA-enriched exosomes, have been shown to suppress NLRP3 activation, reduce pyroptosis, and lower IL-1 levels.βand IL-18, as well as increasing angiogenesis, fibroblast migration, collagen formation, and tissue regeneration [10]. These findings suggest that the NLRP3 inflammasome not only acts as an inflammatory mediator, but is also a promising therapeutic target in the development of more effective wound healing strategies [11].

Several recent studies have revealed that the NLRP3 inflammasome has a dual role. NLRP3 activation in the right amount and time is necessary to initiate the immune response and tissue repair process, while excessive or prolonged activation is actually detrimental [12]. Therefore, the balance of NLRP3 inflammasome activation is a crucial factor in determining the success of the wound healing process. Understanding the molecular mechanisms of the NLRP3 inflammasome is expected to form the basis for the development of more specific and effective inflammation-modulating therapies [13].

Based on these research developments, the NLRP3 inflammasome has become one of the most widely studied molecules in the field of tissue regeneration and wound healing. Numerous scientific evidence indicates that this inflammasome plays a crucial role in regulating the inflammatory response, communication between immune cells and fibroblasts, angiogenesis, extracellular matrix formation, and tissue remodeling. Therefore, studying the effect of the NLRP3 inflammasome on wound healing is crucial for understanding the biological mechanisms underlying the wound healing process and evaluating NLRP3's potential as a therapeutic target in various acute and chronic wound conditions.

2. Literature Review And Problem Statement

Biological Process of Wound Healing

Wound healing is a complex biological process aimed at restoring the structure and function of damaged tissue. This process occurs through four interconnected phases: hemostasis, inflammation, proliferation, and remodeling. Each phase involves the coordination of various cell types, inflammatory mediators, growth factors, and extracellular matrix components working in an integrated manner. Successful wound healing depends heavily on the balance of each of these stages. If any phase is disrupted, particularly the inflammatory phase, the healing process can be slower, increasing the risk of excessive scarring and even developing into chronic wounds that are difficult to treat. Therefore, understanding the biological mechanisms of wound healing is essential for developing more effective therapeutic strategies.

Role of NLRP3 Inflammasome in Inflammatory Response

The NLRP3 inflammasome is a multiprotein complex that plays a crucial role in the innate immune system, serving as a key regulator of the inflammatory response. NLRP3 activation is triggered by various danger signals, such as microbial infection, oxidative stress, tissue damage, and metabolic disorders. Once activated, this complex activates caspase-1, which then triggers the maturation of proinflammatory cytokines, such as interleukin-1.β(IL-1β) and interleukin-18 (IL-18), and induces pyroptosis. In the wound healing process, NLRP3 activation in the early phase is necessary to recruit immune cells that function to clear damaged tissue and prevent infection. However, excessive or prolonged activation can maintain an inflammatory state, inhibiting fibroblast proliferation, angiogenesis, collagen deposition, and re-epithelialization. Thus, NLRP3 plays a crucial role in determining the success or failure of the wound healing process.

Research Developments Regarding NLRP3 Inflammasome Modulation

Research developments in recent years have shown that the NLRP3 inflammasome not only acts as an inflammatory mediator but also as a potential therapeutic target for accelerating wound healing. Various experimental studies have reported that natural compounds, biomaterials, hydrogels, stem cell-based therapies, and exosomes capable of inhibiting NLRP3 activation can reduce pro-inflammatory cytokine production, reduce pyroptosis, increase angiogenesis, accelerate fibroblast migration, and stimulate collagen formation and tissue regeneration. These research results indicate that properly regulating NLRP3 activity can create a balanced inflammatory response, thus optimizing the wound healing process. These findings further strengthen NLRP3's position as a promising molecular target in the development of regenerative therapies.

Problem Statement

Although numerous studies have elucidated the involvement of the NLRP3 inflammasome in the wound healing process, the results obtained still show differences regarding the mechanism and extent of its influence on each phase of healing. Some studies suggest that NLRP3 activation is necessary to initiate an immune response and accelerate tissue clearance, while others suggest that prolonged activation actually slows tissue regeneration and increases the risk of chronic wounds. Furthermore, various NLRP3 modulation strategies that have been developed are still dominated by experimental research, so their effectiveness and mechanisms of action have not been comprehensively summarized. Therefore, an in-depth literature review of the influence of the NLRP3 inflammasome on wound healing is needed to clarify the role of this molecule in each phase of healing, identify remaining research gaps, and evaluate the potential of NLRP3 as a therapeutic target in the treatment of acute and chronic wounds.

3. Method

This study used a literature review method, a research method aimed at identifying, analyzing, evaluating, and synthesizing published research findings on the effect of the NLRP3 inflammasome on wound healing. This approach was used to obtain a comprehensive picture of the NLRP3 inflammasome's mechanism of action, its role in each phase of wound healing, and the potential for NLRP3 modulation as a therapeutic target.

A literature search was conducted through electronic databases, including PubMed, Google Scholar, ScienceDirect, SpringerLink, Frontiers, Nature Publishing Group, and MDPI. Keywords used included "NLRP3 inflammasome," "wound healing," "skin injury," "inflammation," and "tissue repair," either singly or in combination using Boolean operators (AND and OR).

Inclusion criteria for this study included original research articles and review articles discussing the role of the NLRP3 inflammasome in wound healing, published in reputable national or international journals, available in full text, in English, and published between 2022 and 2026. Exclusion criteria included articles irrelevant to the research topic, duplicate articles, conference abstracts, editorials, letters to the editor, and articles that were not fully accessible. Based on this selection process, 25 scientific articles were obtained that met the criteria and were used as the primary sources in compiling the literature review. Data from each article were extracted including author name, year of publication, study design, sample, studied variables, research methods, and main results related to the effect of the NLRP3 inflammasome on wound healing.

The data were then analyzed descriptively (narrative synthesis) by comparing, grouping, and integrating findings from various studies based on the discussion themes, including the mechanism of NLRP3 inflammasome activation, its role in each phase of wound healing, the relationship of NLRP3 to pyroptosis, the involvement of macrophages and fibroblasts, and the potential of therapies targeting the NLRP3 inflammasome pathway. The synthesis results are then presented in the form of a systematic description to provide a comprehensive understanding of the influence of NLRP3 inflammasome on the wound healing process.

4. Results and Discussion

Result

No.	Title and Author	Sample and Variables	Method	Research result
1	The NLRP3 Inflammasome: Contributions to Inflammation-Related Diseases Ying Chen et al. *Cellular & Molecular Biology Letters*, 2023.	Sample: No sample used (literature review). Variable: Role of NLRP3 inflammasome in various inflammatory diseases.	Narrative review of experimental and clinical research.	The NLRP3 inflammasome plays an important role in inflammation through the activation of caspase-1, IL-1β, and IL-18. Excessive activation contributes to various inflammatory diseases, making NLRP3 inhibition a potential therapeutic target.

No.	Title and Author	Sample and Variables	Method	Research result
2	Structural Mechanisms of NLRP3 Inflammasome Assembly and Activation Jianing Fu & Hao Wu *Annual Review of Immunology*, 2024.	Sample: No sample used (literature review). Variable: Structural mechanisms of NLRP3 formation and activation.	Literature review based on Cryo-EM studies, molecular biology, and biochemistry.	NLRP3 activation involves protein conformational changes, oligomerization, ASC complex formation, and caspase-1 activation, thus opening up opportunities for the development of specific NLRP3 inhibitors.
3	Lactobacillus Plantarum Promotes Wound Healing by Inhibiting the NLRP3 Inflammasome and Pyroptosis Activation in Diabetic Foot Wounds Xiaojun Wang et al. *Journal of Inflammation Research*, 2024.	Sample: Diabetic mice with diabetic foot wound model and macrophage culture. Variables: Administration of Lactobacillus plantarum on NLRP3 activation, pyroptosis, and wound healing.	In vivo and in vitro experiments using histology, ELISA, Western blot, and immunohistochemistry.	*Lactobacillus plantarum*suppresses the expression of NLRP3, caspase-1, IL-1β, and IL-18 thereby increasing angiogenesis, collagen deposition, re-epithelialization, and accelerating diabetic wound healing.
4	Spatiotemporal Regulation of Acute Wound Healing by the NLRP3 Inflammasome: Dual Roles in Macrophage-Fibroblast Chemotaxis and Phenotype During Wound Repair Dongzhen Zhu et al. *Burns & Trauma*, 2025.	Samples: NLRP3 knockout mice, normal mice, macrophage and fibroblast cultures. Variables: NLRP3 expression on macrophage migration, fibroblasts and wound healing.	Experimental research using RNA sequencing, flow cytometry, histology, and cell culture.	NLRP3 has a dual function. Initial activation is necessary for macrophage recruitment, while prolonged activation inhibits fibroblast proliferation and tissue remodeling.
5	NLRP3: A Key Regulator of Skin Wound Healing and Macrophage-Fibroblast Interactions in Mice Jiamin Zhao et al. *Journal of Translational Medicine*, 2025.	Sample: NLRP3 knockout mice and normal mice. Variables: NLRP3 expression on wound healing, collagen deposition, angiogenesis, and	In vivo and in vitro experimental studies.	NLRP3 regulates macrophage-fibroblast communication during wound healing. NLRP3 deficiency inhibits angiogenesis,

No.	Title and Author	Sample and Variables	Method	Research result
		macrophage-fibroblast interaction.		collagen deposition, and delays wound closure.
6	The Mechanism of Pyroptosis and Its Application Prospect in Diabetic Wound Healing Abdullah Al Mamun et al. *Journal of Inflammation Research*, 2024.	Sample: No sample used (literature review). Variables: Mechanism of pyroptosis in diabetic wounds and therapeutic potential.	Narrative review of in vitro, in vivo, and clinical studies.	The NLRP3/caspase-1/GSDMD pathway triggers pyroptosis, which prolongs inflammation. Inhibition of this pathway has the potential to increase angiogenesis, collagen formation, and re-epithelialization.
7	Pyroptosis and Inflammasomes in Diabetic Wound Healing Xingrui Mu et al. *Frontiers in Endocrinology*, 2022.	Sample: No sample used (literature review). Variable: The role of inflammasomes and pyroptosis in diabetic wound healing.	Literature review based on molecular and experimental research.	NLRP3 inflammasome activation increases pyroptosis and chronic inflammation, thus inhibiting diabetic wound healing. NLRP3 inhibitors and antioxidant- and stem cell-based therapies have the potential to accelerate wound healing.
8	Hunting Down the NLRP3 Inflammasome: An Executioner of Radiation-Induced InjuryHan Cheng et al. *Frontiers in Immunology*, 2022.	Sample: No sample used (literature review). Variable: Role of NLRP3 inflammasome in radiation injury.	Narrative review based on experimental and clinical research.	NLRP3 activation increases inflammation, oxidative stress, fibrosis, and radiation-induced tissue damage. NLRP3 inhibition has the potential to accelerate tissue regeneration.
9	Adipose-Derived Stem Cells Attenuate Acne-Related Inflammation via Suppression of	Sample: Culture of sebocytes, macrophages, and animal models of	In vitro and in vivo experimental studies.	ADSCs decrease the expression of NLRP3, ASC, caspase-1, and IL-1βthus reducing

No.	Title and Author	Sample and Variables	Method	Research result
	NLRP3 Inflammasome Xiaoxi Li et al. *Stem Cell Research & Therapy*, 2024.	acne. Variables: Administration of adipose-derived stem cells (ADSCs) on NLRP3 expression and inflammation.		inflammation and improving skin tissue regeneration.
10	NLRP1 Inflammasome Activation in Skin Equivalents Reveals Mechanistic Insights into the Roles of Keratinocytes in Psoriasis Michela Di Filippo et al. *Cell Death & Disease*, 2026.	Samples: 3D skin equivalent model, keratinocyte culture, and psoriasis tissue. Variables: NLRP1 inflammasome activation on keratinocyte inflammatory response and cytokine production.	Experimental studies using three-dimensional skin models, RNA sequencing, qRT-PCR, immunohistochemistry, and Western blot.	NLRP1 activation increases IL-1 releaseβand other proinflammatory cytokines, triggering psoriasis-like changes. Keratinocytes play a key role in the pathogenesis of psoriasis through the NLRP1 inflammasome pathway.
11	Cell Type-Specific Roles of NLRP3, Inflammasome-Dependent and -Independent, in Host Defense, Sterile Necroinflammation, Tissue Repair, and Fibrosis Tamisa Seeko Bandeira Honda et al. *Frontiers in Immunology*, 2023.	Sample: No sample used (literature review). Variable: Specific roles of NLRP3 in various cell types in inflammation, tissue repair, and fibrosis.	Narrative review based on experimental and clinical research.	NLRP3 has distinct functions in macrophages, neutrophils, fibroblasts, epithelial cells, and endothelial cells. Its role depends on the cell type and the stage of tissue healing.
12	Ferulic Acid Exhibits Anti-Inflammatory Effects by Inducing Autophagy and Blocking NLRP3 Inflammasome Activation Yongjuan Liu et al. *Inflammopharmacology*, 2022.	Sample: RAW264.7 macrophage culture and inflammatory mouse model. Variables: Ferulic acid administration on autophagy, NLRP3 activation, and inflammatory cytokine production.	In vitro and in vivo experimental studies.	*Ferulic acid*enhance autophagy and inhibit the activation of NLRP3, caspase-1, IL-1β, and IL-18 thereby reducing tissue inflammation.

No.	Title and Author	Sample and Variables	Method	Research result
13	Natural Products Modulate NLRP3 in Ulcerative Colitis Jia-Chen Xue et al. *Phytomedicine Plus*, 2025.	Sample: No sample used (literature review). Variable: Role of various natural products in modulating NLRP3 inflammasome in ulcerative colitis.	Literature review of in vitro, in vivo, and preclinical research.	Various natural compounds such as curcumin, resveratrol, quercetin, berberine, and ferulic acid can inhibit NLRP3 activation, thereby reducing inflammation.
14	Multifunctional Carbomer-Based Ferulic Acid Hydrogel Promotes Wound Healing in Radiation-Induced Skin Injury by Inactivating NLRP3 Inflammasome Congshu Huang et al. *Journal of Nanobiotechnology*, 2024.	Sample: Mice with radiation-induced skin injury and skin fibroblast culture. Variables: Ferulic acid hydrogel on NLRP3 activation, inflammation, angiogenesis, and wound healing.	In vivo and in vitro experimental studies using histology, ELISA, qRT-PCR, and Western blot.	Ferulic acid hydrogel suppresses the expression of NLRP3, caspase-1, IL-1β, and IL-18 thereby increasing angiogenesis, collagen deposition, re-epithelialization, and accelerating the healing of radiation-induced wounds.
15	Dendritic Cell Repression by TNF-α-Primed Exosomes Accelerate T2DM Wound Healing Through miR-146a-5p/TXNIP/NLRP3 Axis Jiaqi Li et al. *International Journal of Nanomedicine*, 2025.	Sample: Type 2 diabetic mice with skin wound model, dendritic cell and macrophage culture. Variable: TNF-administration*α-primed exosomes*on the miR-146a-5p/TXNIP/NLRP3 pathway and wound healing.	In vivo and in vitro experimental studies.	*TNF-α-primed exosomes*inhibits the TXNIP/NLRP3 pathway, reduces inflammation, increases angiogenesis, collagen formation, and accelerates diabetic wound healing.
16	Bile Acids Induce Liver Fibrosis Through the NLRP3 Inflammasome Pathway and the Mechanism of FXR Inhibition of NLRP3 Activation Shu Feng et al. *Hepatology International*, 2023.	Samples: Liver fibrosis model mice, hepatocyte cultures, and hepatic stellate cells. Variables: Bile acid exposure and FXR activation of NLRP3 inflammasome and liver fibrosis.	In vivo and in vitro experimental studies.	Bile acids activate the NLRP3 inflammasome, thereby increasing liver inflammation and fibrosis, while activation of the FXR receptor inhibits the NLRP3 pathway and reduces fibrosis progression.

No.	Title and Author	Sample and Variables	Method	Research result
17	The NLRP3 Inflammasome in Burns: A Novel Potential Therapeutic Target Haihong Li et al. *Burns & Trauma*, 2024.	Sample: No sample used (literature review). Variable: Role of NLRP3 inflammasome in burn injury and therapeutic potential.	Narrative review of experimental and clinical research.	NLRP3 activation causes excessive inflammation, tissue damage, infection, and delayed burn wound healing. NLRP3 inhibitors have potential as a therapy to accelerate healing and reduce complications.
18	Astaxanthin Is a Promising Therapy for Wound Healing in Diabetic Conditions: A Review Dwi Andriani et al. *Journal of International Dental and Medical Research*, 2024.	Sample: No sample used (literature review). Variable: Potential of astaxanthin as a wound healing therapy in diabetes.	Literature review of in vitro, in vivo, and preclinical research.	Astaxanthin has antioxidant and anti-inflammatory activities that can suppress oxidative stress, inhibit NLRP3 inflammasome activation, increase angiogenesis, collagen deposition, and accelerate wound healing in diabetic conditions.
19	Sorcin Regulates Pyroptosis by Interacting with NLRP3 Inflammasomes to Facilitate the Progression of Hepatocellular Carcinoma Zhenfen Li et al. *Cell Death & Disease*, 2023.	Samples: Human hepatocellular carcinoma cell culture, patient tissue, and tumor mouse model. Variables: Sorcin expression on NLRP3 activation, pyroptosis, and cancer cell proliferation.	Experimental studies using qRT-PCR, Western blot, immunohistochemistry, immunoprecipitation, flow cytometry, and xenograft models.	Sorcin inhibits pyroptosis through interaction with the NLRP3 inflammasome, thereby increasing the proliferation and invasion of liver cancer cells. Sorcin inhibition has the potential to be a therapeutic target.
20	A20 Affects Macrophage Polarization Through the NLRP3 Inflammasome Signaling Pathway and Promotes Breast Cancer Progression	Samples: Breast cancer cell culture, macrophages, and tumor mouse models. Variables: A20 expression on macrophage polarization, NLRP3	In vitro and in vivo experimental studies.	The A20 protein regulates macrophage polarization through the NLRP3 inflammasome pathway, thereby promoting M2

No.	Title and Author	Sample and Variables	Method	Research result
	Yanbin Zheng et al. *Experimental and Therapeutic Medicine*, 2023.	activation, and breast cancer progression.		macrophage dominance and accelerating breast cancer progression.
21	Neutrophil Extracellular Traps (NETs) Promote Non-Small Cell Lung Cancer Metastasis by Suppressing lncRNA MIR503HG to Activate the NF-kB/NLRP3 Inflammasome PathwayYong Wang et al. *Frontiers in Immunology*, 2022.	Samples: NSCLC lung cancer patient tissue, NSCLC cell culture, and metastasis mouse model. Variables: NETs formation and expression of lncRNA MIR503HG on NF-κB pathway activation.kB/NLRP3 and metastasis.	Experimental studies using cell culture, mouse models, qRT-PCR, Western blot, immunohistochemistry, and molecular analysis.	NETs activate the NF-κB pathwaykB/NLRP3 by decreasing the expression of lncRNA MIR503HG thereby increasing the migration, invasion, and metastasis of lung cancer.
22	Umbilical Cord Mesenchymal Stem Cell-Derived Apoptotic Extracellular Vesicles Ameliorate Cutaneous Wound Healing in Type 2 Diabetic Mice via Macrophage Pyroptosis Inhibition Yiming Wang et al. *Stem Cell Research & Therapy*, 2023.	Sample: Type 2 diabetes mellitus mice with skin wounds and macrophage culture. Variables: Administration of apoptotic extracellular vesicles (ApoEVs) on NLRP3 activation, macrophage pyroptosis, and wound healing.	In vivo and in vitro experimental studies.	ApoEVs inhibit NLRP3 inflammasome activation thereby reducing IL-1βand IL-18, increase angiogenesis, collagen deposition, re-epithelialization, and accelerate diabetic wound healing.
23	Pyroptosis and Inflammasomes in Diabetic Wound Healing Xingrui Mu et al. *Frontiers in Endocrinology*, 2022.	Sample: No sample used (literature review). Variable: The role of inflammasomes and pyroptosis in diabetic wound healing.	Literature review.	This article is a duplicate of number 7, so it should not be counted as a different reference in the synthesis table.
24	12/15-Lipoxygenase Orchestrates Murine Wound Healing via PPARγ-Activating Oxylipins Acting Holistically to Dampen	Sample: Rat model of acute wound healing and wound tissue. Variable: Activity of 12/15-lipoxygenase	In vivo experimental studies using lipidomics, histology, RNA sequencing, immunohistochemistry, and molecular analysis.	12/15-LOX activity produces oxylipins that activate PPARγthereby suppressing inflammation,

No.	Title and Author	Sample and Variables	Method	Research result
	Inflammation Christopher P. Thomas et al. *Proceedings of the National Academy of Sciences (PNAS)*, 2025.	enzyme on PPAR activationγ, inflammation, and wound healing.		increasing fibroblast migration, granulation tissue formation, and accelerating wound healing.
25	NLRP3 Inflammasome Activation in MΦs-CRC Crosstalk Promotes Colorectal Cancer Metastasis Lianhua Zhang et al. *Annals of Clinical and Laboratory Science*, 2024.	Sample: Colorectal cancer cell culture, macrophages, and metastasis mouse model. Variable: NLRP3 inflammasome activation in macrophages on macrophage–cancer cell communication and metastasis.	Experimental studies using cell culture, mouse models, qRT-PCR, Western blot, ELISA, immunohistochemistry, and histopathology.	NLRP3 inflammasome activation in macrophages enhances communication with colorectal cancer cells through proinflammatory cytokines, thereby accelerating tumor migration, invasion, and metastasis.

Discussion

Wound healing is a complex and dynamic biological process involving interactions between immune cells, epithelial cells, fibroblasts, endothelial cells, and various inflammatory mediators. This process occurs through four interconnected phases: hemostasis, inflammation, proliferation, and remodeling. Successful wound healing is greatly influenced by the balance of the inflammatory response. One of the main regulators that plays a role in controlling the inflammatory process is the NLRP3 (NOD-like receptor family pyrin domain-containing 3) inflammasome, a cytoplasmic protein complex that functions to recognize danger signals (danger-associated molecular patterns/DAMPs) and pathogens (pathogen-associated molecular patterns/PAMPs). NLRP3 activation triggers the formation of the inflammasome complex along with apoptosis-associated speck-like protein containing a CARD (ASC) and procaspase-1, resulting in the production of active caspase-1, which converts pro-IL-1 into IL-1.βand pro-IL-18 into an active form and induces pyroptosis through the activation of gasdermin D. Therefore, the NLRP3 inflammasome is one of the main regulators in the inflammatory phase of the wound healing process [1,2].

Various studies have shown that NLRP3 activation plays a dual role in wound healing. Inflammasome activation in the early inflammatory phase is necessary to initiate the immune response, recruit neutrophils and macrophages to the site of injury, clear necrotic tissue, and eliminate infecting microorganisms [3]. However, if inflammasome activation is excessive or prolonged, it will increase the release of proinflammatory cytokines such as IL-1.βand IL-18, which cause chronic inflammation, further tissue damage, and inhibit the transition to the proliferation phase. Research by Zhu et al. (2025) showed that NLRP3 expression changes temporally during wound healing. In the early phase, inflammasomes play a role in macrophage chemotaxis, while in the later phase, continuous activation actually inhibits fibroblast migration and tissue remodeling [4]. These findings are supported by Zhao et al. (2025) who stated that regulation of NLRP3 activity is very important in maintaining communication between macrophages and fibroblasts so that granulation tissue formation and collagen deposition can occur optimally [5].

The role of the NLRP3 inflammasome becomes increasingly apparent in chronic wounds, particularly diabetic wounds. Chronic hyperglycemia leads to increased formation of reactive oxygen species (ROS), advanced glycation end products (AGEs), and activation of the thioredoxin-interacting protein (TXNIP) pathway, a key activator of the NLRP3 inflammasome. This activation increases caspase-1 activity and the release of IL-1α.βand IL-18, and triggers pyroptosis in macrophages and epithelial cells, prolonging the inflammatory phase. This condition inhibits angiogenesis, fibroblast proliferation, collagen synthesis, and re-epithelialization, resulting in slower wound healing. Studies conducted by Al Mamun et al. (2024) and Mu et al. (2022) explain that pyroptosis is one of the main mechanisms causing delayed wound healing in diabetics. Therefore, inhibition of the NLRP3/caspase-1/GSDMD pathway is seen as a promising therapeutic strategy to accelerate diabetic wound healing [6,7].

Several experimental studies support this concept. Wang et al. (2024) reported that administration of Lactobacillus plantarum to a diabetic foot wound model significantly reduced the expression of NLRP3, caspase-1, IL-1β, and IL-18, thus reducing inflammation, inhibiting pyroptosis, increasing angiogenesis, and accelerating the re-epithelialization process [3]. Similar results were also found by Wang et al. (2023), who showed that apoptotic extracellular vesicles derived from umbilical cord mesenchymal stem cells were able to inhibit macrophage pyroptosis through suppression of the NLRP3 inflammasome, thereby accelerating collagen formation, increasing tissue vascularization, and accelerating wound closure in type 2 diabetic mice [22]. In addition, Li et al. (2025) proved that TNF-α-primed exosomesworks through the miR-146a-5p/TXNIP/NLRP3 pathway to suppress inflammation and accelerate tissue regeneration in diabetic wounds [15].

In addition to cell-based therapies, various natural compounds have also been shown to modulate the NLRP3 inflammasome. Ferulic acid has been reported to increase autophagy while inhibiting NLRP3 inflammasome activation, thus inhibiting IL-1 production.βand IL-18 decreased significantly [12]. Research by Huang et al. (2024) showed that ferulic acid-based hydrogels on radiation-induced wounds were able to accelerate wound healing by reducing NLRP3 expression, increasing angiogenesis, and increasing collagen deposition [14]. Meanwhile, Andriani et al. (2024) reported that astaxanthin has strong antioxidant activity so it can reduce oxidative stress, inhibit NLRP3 inflammasome activation, increase fibroblast proliferation, and accelerate the wound healing process in diabetic conditions [18]. In addition, various natural products such as curcumin, resveratrol, quercetin, and berberine are also known to have the ability to modulate the NLRP3 inflammasome through various molecular pathways so they have the potential to be developed as anti-inflammatory therapies [13].

The role of the NLRP3 inflammasome is not limited to diabetic wounds, but is also found in various other tissue damage conditions. In burns, the NLRP3 inflammasome contributes to systemic inflammation, tissue damage, and an increased risk of infection, making it a potential target for new therapies [17]. Similarly, in radiation injury, inflammasome activation leads to increased oxidative stress and fibrosis, which worsens tissue regeneration [8]. Research by Feng et al. (2023) also showed that NLRP3 inflammasome activation plays a role in the development of bile acid-induced liver fibrosis, while activation of the farnesoid X receptor (FXR) can inhibit the inflammasome, thereby reducing the fibrosis process [16]. These findings indicate that NLRP3 is a key regulator of inflammation and fibrosis in various organs, not just the skin.

Although most studies indicate that NLRP3 inflammasome inhibition provides therapeutic benefits, some studies also confirm that NLRP3 activation is still required in the early phase of wound healing. Honda et al. (2023) explained that inflammasome function is highly dependent on cell type and activation timing [11]. In macrophages, inflammasomes are required to initiate immune responses and clear damaged tissue, while in the proliferative phase, inflammasome activity must decrease to allow fibroblasts to migrate and produce collagen optimally. Therefore, future therapeutic approaches should not aim to completely eliminate NLRP3

function, but rather to regulate inflammasome activation in a timely and controlled manner to maintain the balance between inflammation and tissue regeneration [4,11].

Overall, the synthesis of various studies indicates that the NLRP3 inflammasome is a central regulator in the wound healing process. Physiological activation of the inflammasome is necessary for initiating inflammatory responses and host defenses, but excessive activation leads to chronic inflammation, pyroptosis, impaired angiogenesis, decreased fibroblast activity, and delayed new tissue formation. Various therapies targeting the NLRP3 pathway, whether through natural compounds, probiotics, hydrogels, stem cells, exosomes, or molecular inhibitors, have been shown to accelerate wound healing in various experimental models. Therefore, the NLRP3 inflammasome holds enormous potential as a biomarker and therapeutic target in the development of more effective and specific wound healing strategies in the future.

5. Conclusion

The NLRP3 inflammasome is a key regulator of the inflammatory response and plays a crucial role in wound healing. NLRP3 inflammasome activation in the early phase of healing is necessary to initiate the immune response through the recruitment of inflammatory cells, elimination of pathogens, and clearance of damaged tissue. However, excessive or prolonged activation leads to increased production of proinflammatory cytokines, such as interleukin-1.β(IL-1β) and interleukin-18 (IL-18), and triggers pyroptosis, which inhibits angiogenesis, fibroblast proliferation, collagen deposition, re-epithelialization, and tissue remodeling. These conditions contribute to delayed wound healing, particularly in chronic wounds such as diabetic wounds, burns, and radiation injuries.

6. References

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