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A Comprehensive Review of Modulation of Inflammation in Wound Healing: Phases, Pathway, And Treatment Approaches

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Abstract

Wound healing is a complex, multi-phase process in which the regulation of inflammation is critical for successful tissue repair. Anti-inflammatory agents play a pivotal role by modulating the inflammatory response, preventing excessive tissue damage, and promoting the transition from the inflammatory to the proliferative and remodeling phases. Both endogenous mediators, such as IL-10 and IL-4, and exogenous agents including natural products, pharmacological compounds, and advanced biotherapies like mesenchymal stem cells (MSCs) have demonstrated the ability to suppress pro-inflammatory cytokines and enhance anti-inflammatory pathways, thereby accelerating wound closure and improving tissue regeneration. However, the inappropriate use of certain anti-inflammatory drugs, such as glucocorticoids, may impair healing by excessively dampening necessary immune responses. Recent advances highlight the importance of balancing inflammation through targeted therapies that optimize immune cell activity, cytokine signaling, and extracellular matrix remodeling. Continued research into the mechanisms and clinical applications of anti-inflammatory agents holds promise for improving outcomes in both acute and chronic wound management.

Introduction

The wound healing cascade is greatly impacted by the quick and intricately coordinated process of wound inflammation. Inflammatory, proliferation, and maturation stages are among the processes that follow damage and result in wound closure and the return of normal skin integrity. Tissue injury and pathogenic microbial infections are examples of stimuli that might stress the host immune system or trigger an inflammatory response. Numerous pieces of evidence support the beneficial role of inflammation, which is necessary to both eliminate dead tissues from the site of damage and defend against the invasion of invasive pathogens. In addition to its beneficial effects, chronic inflammation can be harmful and cause dysregulated phases of wound healing, which can leave too much scarring. Finding equilibrium in the inflammatory cascade is one of the most difficult things to do when creating a medication to cure wounds **[28].**

The general phases of the wound healing process have been identified by experimental studies conducted over the past 20 years. Three consecutive, overlapping phases have been used to organize this intricate network. The inflammatory phase begins with an instantaneous reaction to damage; primary sensory neurons detect damage and alert the brain to danger, which stops the bleeding and initiates inflammation. Eliminating the pathogens and cleaning the wound are the next goals of the inflammatory phase, which is headed by peripheral blood mononuclear cells. After this is finished, equilibrium is restored and the inflammatory phase is over. The second phase, known as the proliferative phase, is to start tissue remodeling and heal wound damage. The main activities of this phase include fibroplasia, re-epithelialization, angiogenesis, and peripheral nerve repair. Last but not least, restoring skin integrity and finishing tissue remodeling are the goals of the last stage. The current state of the participant cells, extracellular matrix, cytokines, chemokines, and growth factors, as well as how they interact with the milieu during the wound healing process, are all covered in this review **[2].**

Effective therapies development in the field of wound healing depends on an understanding of the intricate interactions between pro- and anti-inflammatory cytokines. Pro-inflammatory cytokines such as IL-1β, IL-6, TNF-α, and other chemokines are essential for attracting cells for debris removal and growth factor recruitment during the early phases of wound healing. For the best wound healing, this early inflammation must be carefully controlled and resolved quickly. Anti-inflammatory proteins like IL-10 and IL-4 play a crucial role in easing the healing process's progression to later phases, when pro-inflammatory cytokines encourage angiogenesis and wound remodeling. This viewpoint highlights the intricacy of inflammatory cytokines in the study of wound healing and the necessity of thorough and objective approaches in their assessment **[18].**

Type of Wound Healing

1. Chronic Wounds: Wounds brought on by metabolic problems are known as chronic wounds. In contrast to acute wounds, which heal in a balanced and brief amount of time, these wounds require a long time to recover. The synthesis and breakdown of cells and extracellular matrix (ECM), such as collagen, are out of balance in chronic wounds. These wounds are often divided into three groups:

(1) venous/vascular ulcers,

(2) Diabetic ulcers, Wound.

(3) Pressure ulcers. Another category is also included in chronic wounds called as ischemic wounds **[21]**.

i. Venous/Vascular: More than 70% of chronic wounds are ulcers, often referred to as stasis ulcers or dermatitis, which are a type of chronic wound that affects the lower extremities, or legs. V/V ulcers are primarily caused by inflammatory mechanisms that include leukocyte activation, endothelial damage, platelet aggregation, and intracellular edema. These disorders typically occur in old age due to deep vein thrombosis, obesity, or prior injury **[16,23].**

ii. Diabetic Wounds: These wounds are primarily produced by an impaired immune system and neuropathic disorders, which are both consequences of diabetic diseases. Because of neuropathy and weakened immune systems, a little skin damage goes undetected in both of these disorders. The body is unable to stop infections, and a minor lesion eventually turns into a chronic one. The third type of chronic wounds that commonly develop in patients with paralytic disorders are pressure ulcers. The immobility of paralysis causes tissues to become ischemic, which restricts blood flow to certain tissues, primarily muscles, as the pressure on the tissue increases relative to capillaries. Ischemic Another kind of chronic wound is one that is brought on by a limitation in the blood flow to the tissues, which leaves the tissues without the oxygen and glucose needed for cellular function **[37].**

2. Acute Wound: Acute wounds are those brought on by environmental conditions that involve a traumatic damage. These wounds heal in an orderly fashion because of the exact and correct balance between cell and extracellular matrix synthesis and breakdown. Based on the kind of environmental elements that contributed to the damage, acute wounds are divided into several kinds. Acute wounds are often divided into two groups: surgical wounds and traumatic wounds. The literature has identified the following six types of acute traumatic or surgical wounds **[4,8].**

Pathophysiology of wound healing

In order to avoid infection and fluid loss, the ultimate goal of the skin's wound healing process is to quickly restore the barrier to the external environment. Numerous growth factor and cytokine signaling cascades are involved in wound healing, which aids in the removal of infection from the wound and the reconstruction of damaged skin. On the other hand, prolonged healing and the development of chronic wounds may occur if these four steps are disturbed or altered. Amputations may be necessary in the worst situations due to chronic wounds that take months to heal or never heal at all. This chapter explains the wound healing process as well as the several triggers that can lead to the development of pressure injuries, diabetic ulcers, and arterial and venous ulcers. Since the number of senior individuals in our society is rising and the number of wounds in the community is at an all-time high, the impact of age on healing responses is examined. Last but not least, wound infection is discussed since it is become more common and poses a serious problem for wound care because of the rising incidence of antibiotic resistance. All things considered, these difficulties are creating an urgent demand for better therapies and therapeutic methods for wound care **[20].**

Phases of wound healing: The process of wound healing is dynamic and intricate, requiring the cooperation of several cellular and molecular processes. The four overlapping stages of hemostasis, inflammation, proliferation, and remodeling can be used to broadly categorize it. Each stage, which is controlled by a complex interaction of cytokines, growth factors, and cell types, is essential to the effective advancement of healing.

1.Hemostasis phase

Coagulation and hemostasis work quickly after damage to shield the vascular system and stop excessive blood loss, ensuring that important organs continue to operate. While reflex vasoconstriction reduces bleeding in the short term, long-term hemostasis requires the coagulation cascade to be activated in order to create a stable fibrin clot. When platelets and blood components come into contact with exposed collagen at the wound site, platelets aggregate and clotting factors are released, starting this process. In addition to halting bleeding, the ensuing clot—which is made up of fibrin and other matrix proteins offers a temporary scaffold for cell migration that is necessary for later stages of healing. Growth factors and cytokines, including PDGF and TGF-β, are secreted by platelets within the clot, attracting and activating neutrophils, macrophages, endothelial cells, and fibroblasts. Furthermore, serotonin and other vasoactive amines generated from platelets raise vascular permeability, which promotes tissue edema and the inflammatory response. The initial inflammatory phase is further intensified by eicosanoids and other lipid mediators released from damaged cell membranes, which paves the way for successful tissue repair **[33].**

2. Inflammatory phase

The second stage of wound healing, inflammation, starts within the first 24 hours after an injury and can persist up to two weeks for typical wounds and much longer for chronic wounds that don't heal. Damaged blood arteries narrow and blood coagulates during the vascular inflammatory response to injury, creating a fibrin network containing aggregating platelets and thrombocytes. In addition to restoring hemostasis and serving as a barrier against microorganisms, this network offers a transient matrix that promotes fibroblast proliferation and cell migration, both of which are essential for reestablishing the skin's defensive role. Rapid leukocyte infiltration during the inflammatory phase causes apparent edema and redness at the wound site, usually within the first 24 hours and continuing for up to two days. Chemokines and cytokines are released when resident immune cells, including mast cells, gamma-delta cells, and Langerhans cells, are activated early. This intensifies the inflammatory response. Because inflammatory cells produce lysosomal enzymes and reactive oxygen species to aid in tissue cleanup and get the wound ready for later healing stages, this localized inflammation is crucial for removing debris and pathogens **[12].**

3. Proliferative phase

The proliferative phase, which can continue up to three weeks in a healed cutaneous lesion, begins when enough fibroblasts move to the site within two to three days following the original damage. Fibroblasts are important during this stage because they produce a lot of immature type III collagen and disordered collagen into this temporary matrix. Under the influence of certain cytokines, fibroblasts that have been attracted to the wound may change into myofibroblasts, which may ultimately cause the wound to constrict and produce more collagen. Numerous signaling pathways, both canonical and noncanonical, have been linked to influencing the wound healing process. These include, but are not limited to, angiotensin II and TGF-β **[1].**

4. Remodeling phase

Permanent scar tissue replaces granulation tissue during the last remodeling stage of wound healing. After four to five weeks of continuous net collagen formation, type I fibrillar collagen gradually replaces type III reticular collagen throughout the course of the next year. Tissue remodeling relies heavily on zinc-dependent endopeptidases, sometimes referred to as matrix metalloproteinases, which are released by epidermal cells. From 3% in the first week to 20% in the third, wound tensile strength keeps rising as collagen synthesis rises. Tensile strength of intact skin peaks at 80% three months after injury, but it never reaches 100%. For the wound healing process to be successful, each of these stage hemostasis/inflammation, proliferation, and remodeling is essential **[1].**

Inflammatory mechanisms in the wound healing process

The process of wound healing is intricately regulated and depends on the interaction of many cells, growth factors, and signaling molecules. It goes through three phases that overlap: remodeling, proliferative, and hemostatic/inflammatory. Tissue damage initiates the first hemostatic/inflammatory phase, which results in platelet aggregation and vasoconstriction, which quickly forms a blood clot and stops bleeding while simultaneously providing a scaffold for cell migration. Histamine and leukotrienes, two mediators produced by mast cells, enhance blood vessel permeability and draw immune cells to the wound site. As the first immune cells to arrive, neutrophils respond to chemotactic cues and use phagocytosis and the release of neutrophil extracellular traps (NETs) to eradicate infections. Monocytes go to the site and develop into macrophages when the inflammation subsides. Early on, M1 macrophages maintain the inflammatory response and help eliminate pathogens; as they develop into the M2 phenotype, they assist tissue healing by releasing growth factors and anti-inflammatory cytokines that encourage angiogenesis and cell proliferation. Presenting antigens to T cells, which change from a pro-inflammatory Th1 response to an anti-inflammatory Th2 profile as healing advances, dendritic cells further regulate the immune response. Additionally, Th17 and regulatory T cells support homeostasis, encourage tissue regeneration, and balance inflammation. Tissue integrity is effectively repaired and restored thanks to this complex cellular and molecular choreography **[10].**

Anti-Inflammatory Therapeutic Strategies

1.Biological Approaches

A wound requires several steps and takes a long time to heal. The main factor causing tissue regeneration and repair processes after tissue damage is inflammation. Therefore, the regulation of inflammation is essential to the pathophysiological processes including skin injury, healing, and remodeling. Because of their immunomodulatory and paracrine qualities, mesenchymal stem cells (MSCs) constitute a novel and potent therapeutic alternative for wound healing. Transplanted MSCs have been demonstrated to accelerate the healing process by using immunomodulation to regulate the inflammatory milieu of wounds. The activation of T cells, natural killer (NK) cells, and dendritic cells (DCs) may be altered, in addition to additional immunomodulatory strategies such as managing neutrophil activity and altering macrophage polarization. Additionally, a number of studies have demonstrated that pretreating MSCs enhances their capacity to regulate immunity. In this review, we provide an overview of the current understanding of how MSCs affect local inflammation in wounds via regulating immunity to promote healing. We also give a summary of methods for maximizing MSCs' usage in wound care **[10].**

2. Pharmacological Agents

1. Nonsteroidal anti-inflammatory drugs (NSAIDs):

The most widely known medications in the world for treating pain, inflammation, and fever are nonsteroidal anti-inflammatory medicines, or NSAIDs. NSAIDs are frequently used to treat ischemic cerebrovascular disorders, osteoarthritis, rheumatoid arthritis, inflammatory illnesses, and dysmenorrhea. These medications work by preventing the creation of prostaglandins. NSAIDs have a number of pharmacologic characteristics. They are mostly organic acids with pKa values between 3 and 5. Mostly carboxylic acids or enols, they have an acidic group. For COX inhibitory action to occur, the acidic moiety is necessary **[29].**

Mechanism of action of NSAIDs:

The suppression of prostaglandin (PG) production is the basis for NSAIDs' mode of action. PG, which is produced from arachidonic acid, is one of the primary mediators of fever, pain, and inflammation. The enzyme cyclooxygenase (COX), formerly known as PGH synthase, catalyzes the reaction. By binding to and inhibiting COX, NSAIDs prevent the synthesis of PG. In animal pain models, it has been shown that PGE1 and PGF2 interfere with the analgesic action of NSAIDs. Because NSAIDs can prevent PG-mediated cerebral vascular dilatation, it has also been shown that they reduce pain. Numerous investigations have demonstrated that NSAIDs work by inhibiting the formation of PGE2 in and around the preoptic hypothalamic region in the circumventricular organs **[29].**

2. Corticosteroids

Corticosteroids, which include glucocorticoids and mineralocorticoids, are a class of steroid hormones released by the adrenal cortex1. That being said, glucocorticoids are commonly known as "corticosteroids." Named for its effect on the metabolism of carbohydrates, glucocorticoids regulate several cellular functions, including as development, inflammation, homeostasis, metabolism, and cognition. Glucocorticoids are currently used therapeutically to treat a wide range of inflammatory and autoimmune diseases, such as multiple sclerosis, septic shock rheumatoid arthritis, asthma, allergies, and inflammatory bowel disease. Unfortunately, the therapeutic benefits of glucocorticoids are limited by the adverse side effects associated with high doses (used to treat SLE and systemic vasculitis) and extended use. Among these negative consequences include osteoporosis, skin atrophy, diabetes, abdominal obesity, glaucoma, cataracts, avascular necrosis and infection, growth retardation, and hypertension **[26].**

Mechanism of action

In addition to being used in short-term therapy for disorders like gout or as intra-articular injections for tendinitis and osteoarthritis, glucocorticoids are commonly utilized for the long-term management of the majority of autoimmune diseases. Their capacity to lower the expression of genes triggered by cytokines accounts for their strong anti-inflammatory properties. Glucocorticoids reach the nucleus after attaching to cytoplasmic steroid receptors and block transcription factors that trigger proinflammatory cytokines, including AP-1 and NF-κB. They also downregulate molecules including ICAM-1, inducible nitric oxide synthase, and COX-2, and repress genes linked to T cell growth and inflammatory mediators. On the other hand, glucocorticoids efficiently reduce inflammation at several molecular levels by upregulating the expression of anti-inflammatory genes such as IL-10 and the IL-1 type 2 decoy receptor **[7].**

3. Natural and Synthetic Materials

In biomedical applications, hydrogels have shown great promise, especially in the treatment of wounds. Their anti-inflammatory qualities have been greatly improved recently, making them useful in treating the chronic inflammation frequently observed in severe burns and diabetic ulcers. Resolving excessive inflammation is essential for proper repair since it frequently interferes with the wounds' normal healing process. The development of hydrogel dressings that effectively scavenge free radicals, sequester chemokines, and encourage the transition of macrophages from the pro-inflammatory M1 to the anti-inflammatory M2 phenotype has been the focus of study over the last five years. These systems aid in controlling inflammation and hastening the healing process. In addition to addressing current issues in the area, this study emphasizes cutting-edge anti-inflammatory hydrogel dressings, talks about unique preparation and application techniques, and lists essential characteristics needed for the best possible wound healing **[14].**

Treatment of Wound Healing

1.Natural Herbals and Spices in Wound Healing

Since ancient times, traditional medicine has used herbal remedies to hasten the healing of wounds. Numerous plants and their preparations, such as Aloe vera, Calendula officinalis, Curcuma longa, and others, have been used traditionally to treat wounds because of their enormous capacity to influence wound healing **[13].** Through a number of methods, plant-based extracts and/or isolates promote tissue regeneration; these processes frequently complement one another to enhance the healing process as a whole **[19].** Wound healing is one of the many disorders that may be managed with natural products and their pure components, which are a growing source of alternative pharmaceutical compounds **[22,24,25]**.

Aloe vera: The perennial herb Aloe vera (Aloe barbadensis Miller) is well known for its therapeutic and cosmetic properties, mostly because of its mucilaginous gel, which is abundant in vitamins, enzymes, polysaccharides, polyphenols, and hormones. It has been used traditionally to treat a variety of skin disorders, including inflammation and wound healing. The ability of aloe vera to treat wounds is still being studied, and there is evidence that its bioactive components aid in tissue repair by affecting immune response, cell migration, and the creation of extracellular matrix **[34].**

Curcuma longa: Also referred to as turmeric, this perennial herb is utilized as a spice and traditional medicine, especially for inflammatory diseases, due to its rhizome. Turmeric's main bioactive ingredient, curcumin, is a polyphenolic antioxidant that gives it several health advantages. Turmeric's 2–5% curcumin has been the subject of much research due to its anti-inflammatory, antioxidant, and wound-healing qualities. By decreasing histamine synthesis and boosting the body's natural anti-inflammatory hormone, cortisol, it has anti-inflammatory properties. Curcumin has therapeutic potential at all phases of wound healing since it also suppresses important inflammatory mediators including NF-kB, TNF-alpha, and IL-1 **[34].**

2. Biological Based Treatments

Burns and other wounds have long been treated with cryopreserved human cadaver skin (used in the UK), human amniotic membrane, and frog skin (used in other countries). Growth factors and artificial skin replacements have been created more recently to aid in the healing of chronic wounds that do not heal, regardless of the cause. These therapies restore lost tissue in the case of skin replacements and focus on various phases of the healing process. To promote the healing of such wounds, a number of growth factors proteins that coordinate and regulate a number of interconnected processes during wound healing produced via recombinant DNA technology have also been created **[27].**

3. Cell and matrix based treatments

It has been demonstrated that autologous fibroblasts seeded onto a hyaluronic acid-derived matrix may effectively heal venous leg ulcers and diabetic foot ulcers. Dermal replacement in such wounds has been accomplished with the use of allogenic fibroblasts, which are derived from newborn human foreskin and cultivated in vitro. They are either sown on nylon mesh or a scaffold that is biologically absorbable. Collagen, matrix proteins, and growth factors are secreted by the proliferating fibroblasts to aid in the healing process. Although the majority of the data to yet comes from treating diabetic foot ulcers and burns, they are intended to give skin restoration in a range of wounds **[27].**

4. Cellular and Molecular Pathways

TGF-β signaling pathway

Through its three isoforms, each of which has a unique temporal impact, TGF-β is a crucial growth factor in wound healing, coordinating inflammation, proliferation, and re-epithelialization. TGF-β, which is released quickly after injury, attracts immune cells and then activates fibroblasts, keratinocytes, and endothelial cells, encouraging the deposition of collagen and extracellular matrix (ECM) and angiogenesis. By increasing Treg cells, suppressing T, B, and NK cells, and influencing macrophages to adopt an anti-inflammatory M2 phenotype through SMAD-dependent and alternative signaling pathways, it also controls immunological responses. Excessive or insufficient disruption of TGF-β signaling can lead to persistent wounds, fibrosis, or poor healing, therefore correct control is crucial. Although therapeutic approaches such as ligand traps, neutralizing antibodies, and recombinant isoforms have the potential to improve healing or lessen fibrosis and scarring, their wide-ranging physiological effects require careful targeting to reduce side effects. Therefore, two major obstacles for upcoming wound healing treatments are preserving TGF-β at physiological levels and enhancing delivery specificity.

VEGF: An important proangiogenic agent that promotes angiogenesis, the creation of granulation tissue, and wound closure, VEGF is essential for epidermal restoration. Hypoxia, pro-inflammatory cytokines, and tissue damage all cause their expression to increase in wound sites, especially when HIF-1α is activated. The serious effects of VEGF shortage demonstrate how important VEGF is for efficient healing and is generated by a variety of cell types, including smooth muscle cells, keratinocytes, endothelial cells, and immune cells. Reduced VEGF levels are frequently seen in chronic wounds, such as those linked to diabetes, which inhibit angiogenesis and postpone healing. By promoting chemotaxis and the development of new blood vessels, VEGF supplementation has demonstrated promise in hastening the healing process in such wounds, particularly diabetic foot ulcers **[36].**

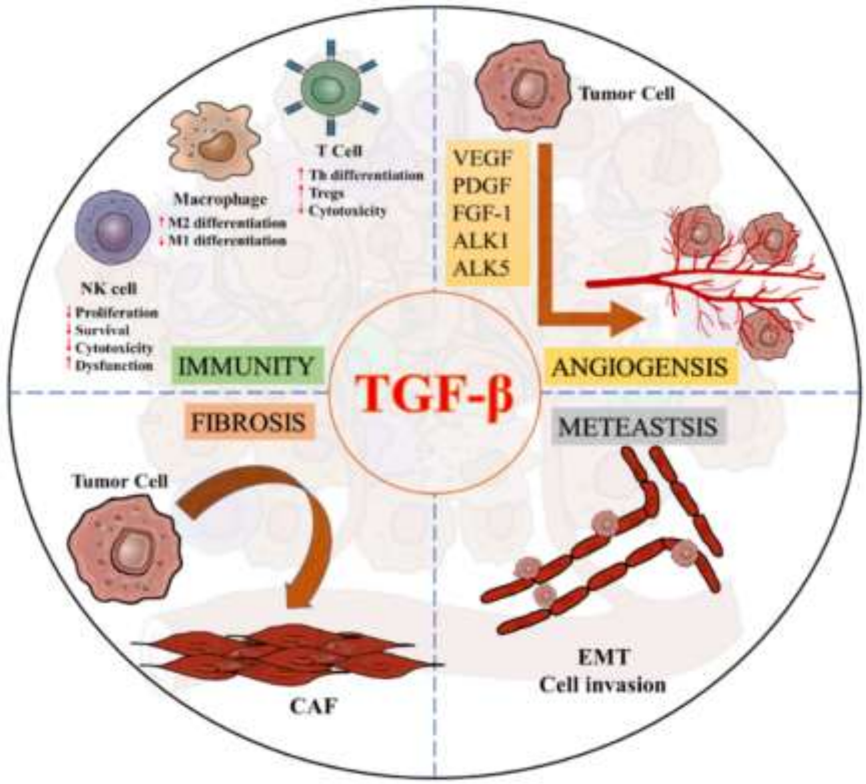

Fig:1 TGF-β signaling pathway

IL-1 signaling pathway

One important pro-inflammatory cytokine, IL-1, stimulates pain sensitivity, fever, vasodilation, and the migration of immune cells to injury sites, all of which contribute to the acute inflammatory response **[32].** Keratinocytes, macrophages, and other immune cells generate its two primary isoforms, IL-1α and IL-1β **[6].** While IL-1α is found in healthy tissue, IL-1β is brought on by illness or stress. Both isoforms increase inflammation by activating the IL-1 receptor complex, which in turn activates the NF-κB and MAPK pathways **[11].** Excessive or extended IL-1 activity can result in chronic wounds, even though it is necessary for starting immune defense and wound healing. By inhibiting IL-1 signaling, the natural IL-1 receptor antagonist (IL-1Ra) reverses this effect **[30].** Treatments that use IL-1Ra, including anakinra, have demonstrated promise in promoting wound healing and lowering inflammation in chronic and infected wounds **[31].** Therefore, focusing on the IL-1/IL-1Ra axis is a viable approach to improving wound healing, especially in chronic or non-healing wounds **[3].**

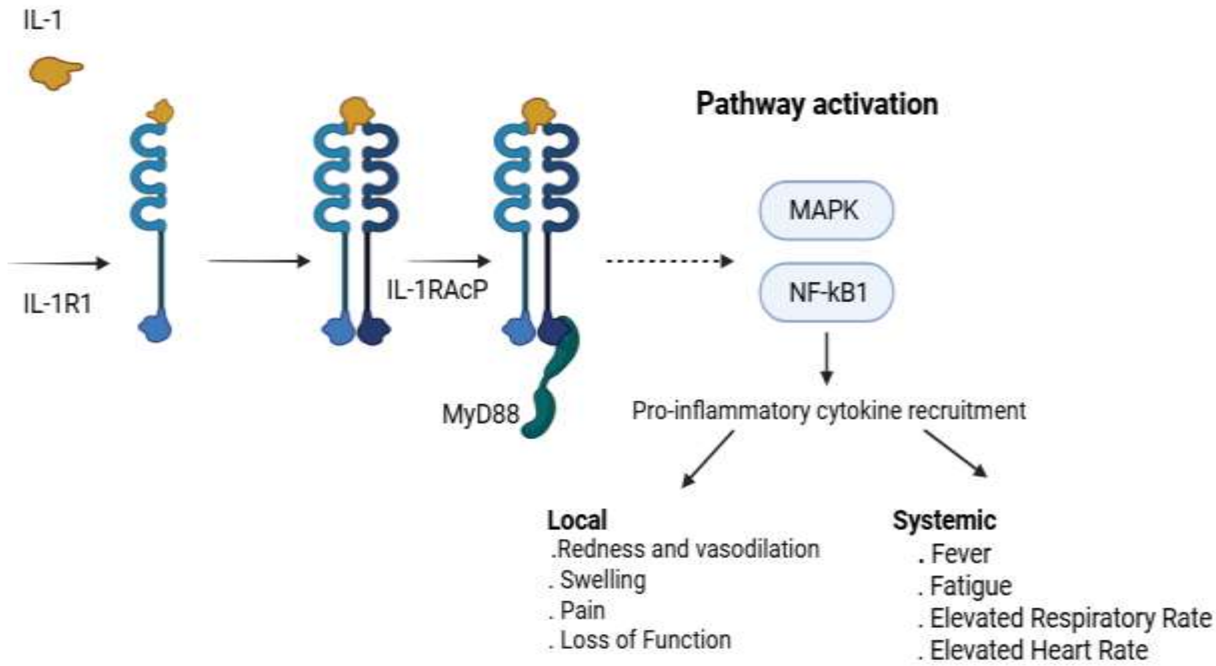

Fig:2 IL-1 signaling pathway

Clinical Significance, Implications and Evidence

Disruption during any wound-healing phase can lead to excessive wound healing or chronic wound formation.

Excessive Wound Healing

Excessive wound healing has an unclear pathophysiology. Continuous localized inflammation, excessive collagen synthesis, aberrant collagen turnover, and excessive extracellular matrix buildup are the hallmarks of this disorder, which is an aberrant type of wound healing. Excessive wound healing can result in hypertrophic and keloid scars **[35].**

Chronic Wound Formation

Any wound that has not healed after four weeks is considered chronic. Some medical practitioners, however, would rather wait three months before making a chronic wound diagnosis **[15].** Age, immunological condition, malnourishment, infection, inadequate oxygenation or perfusion, smoking, illnesses, drugs, radiation, and chemotherapy are the main risk factors for the development of chronic wounds **[9].** Vascular ulcers (venous or arterial ulcers), diabetic ulcers, and pressure ulcers are the most prevalent types of chronic wounds **[5].**

This study used a prospective longitudinal design and electronic wound care data to evaluate the effects of different drugs on the healing times of leg ulcers and acute wounds. The average healing period for 2,089 acute wounds in 1,732 individuals was 35 days. The only drug that was substantially linked to delayed healing was chemotherapy, which prolonged recovery by 21 days. Acute wound healing periods were not significantly impacted by other drugs, such as NSAIDs, corticosteroids, anticoagulants, or antibiotics. The average healing period for 370 leg ulcers in 264 individuals was 73 days. Anticoagulants and NSAIDs were linked to prolonged healing periods, whereas antibiotics and corticosteroids exhibited non-significant tendencies toward quicker healing. However, none of the drug classes had a substantial impact on recovery. With the exception of chemotherapy in acute wounds, the majority of drugs had no discernible effect on the length of time it took for wounds to heal **[17].**

Future Prospects of Anti-Inflammatory Strategies in Wound Healing.

- Smart dressings with sensors will monitor wounds and deliver anti-inflammatory agents as needed.
- Nanotechnology will enable targeted delivery of anti-inflammatory drugs, improving efficacy and reducing side effects.
- Stem cell therapies, especially mesenchymal stem cells, will be used to modulate inflammation and promote tissue regeneration in chronic wounds..
- Advanced biomaterials, such as bioactive hydrogels, will support scar-free healing by mimicking the natural extracellular matrix and delivering anti-inflammatory molecules.
- Small molecule inhibitors targeting specific inflammatory pathways (e.g., MMP-9 inhibitors) will be developed for precise control of wound inflammation.
- Overall, future strategies will focus on personalized, adaptive, and technology-driven wound care to optimize inflammation control and healing outcomes.

Conclusion

In conclusion, the regulation of inflammation is central to effective wound healing, influencing every stage from initial tissue repair to final remodeling. While acute inflammation is necessary for pathogen defense and debris clearance, prolonged or excessive inflammation can impede healing and contribute to chronic wounds or poor scar outcomes. Anti-inflammatory agents including pharmacological drugs like doxycycline, natural compounds such as curcumin, advanced biomaterials, and cell-based therapies have demonstrated the ability to modulate the wound environment, reduce harmful cytokine activity, and promote tissue regeneration. Innovations such as anti-inflammatory hydrogel dressings and nanomaterials further enhance localized therapy, accelerating healing and minimizing complications. However, the effectiveness of these interventions depends on precise timing, appropriate dosing, and consideration of wound-specific factors. Continued research into the molecular mechanisms and targeted delivery of anti-inflammatory agents will be essential for optimizing wound care and improving clinical outcomes for both acute and chronic wounds.

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