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Moringa oleifera Lam. to accelerate wound healing: a review

Fidi Bhawana Jaya¹, Mas Rizky Anggun Adipurna Syamsunarno^{1,2}, Edhyana Sahiratmadja^{1,2}

¹Graduate School of Master Program in Anti-Aging and Aesthetic Medicine, Faculty of Medicine, Universitas Padjadjaran, Indonesia, ²Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Indonesia

ABSTRACT

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An injury to the skin that disrupts the soft tissue may form a wound. The healing process in response to injury is a dynamic and well-regulated process of cellular, humoral, and molecular mechanisms that consists of four partly overlapping phases: hemostasis, inflammation, proliferation, and remodeling. An impaired wound-healing process may cause a formation of an abnormal scar and chronic wounds, leading to a reduced life quality. Therefore, it needs an optimal prevention strategy. Many modalities have been claimed to accelerate wound healing. The trend of using natural products is increasing in most Southeast Asian countries due to their biodiversity. Nowadays, studies on natural compounds are increasing to accelerate wound healing. *Moringa oleifera* Lam. is a high-value plant that each part of it has a high nutritional value as well as a great range of medicinal uses, including anti-inflammatory, antimicrobial, antioxidant, and wound healing properties. In this review, we have explored the *M. oleifera* that are very rich in vitamins, minerals, fatty acids, and phytochemical compounds like quercetin, kaempferol, and vicenin-2, that play a role in the wound healing process. Moreover, these compounds may enhance the healing of wounds with pathological conditions such as diabetes, immunocompromised and persistent infection.

ABSTRAK

Cedera pada kulit yang mengganggu jaringan lunak dapat membentuk luka. Proses penyembuhan sebagai respons terhadap cedera adalah proses yang dinamis dan diatur dengan baik dari mekanisme seluler, humoral, dan molekuler yang terdiri dari empat fase yang saling tumpang tindih: hemostasis, inflamasi, proliferasi, dan remodeling. Gangguan pada proses penyembuhan luka dapat menyebabkan pembentukan jaringan parut abnormal dan luka kronis, yang menyebabkan penurunan kualitas hidup. Oleh karena itu, diperlukan strategi pencegahan yang optimal. Banyak modalitas telah diklaim dapat mempercepat penyembuhan luka. Tren penggunaan produk alami meningkat di sebagian besar negara Asia Tenggara karena keanekaragaman hayatinya. Saat ini, penelitian tentang senyawa alami untuk mempercepat penyembuhan luka semakin meningkat. *Moringa oleifera* Lam. adalah tanaman bernilai tinggi yang memiliki nilai gizi tinggi serta berbagai kegunaan obat, termasuk sifat anti inflamasi, antimikroba, antioksidan, dan untuk penyembuhan luka. Dalam ulasan ini, kami telah mengeksplorasi *M. oleifera* yang sangat kaya akan vitamin, mineral, asam lemak dan senyawa fitokimia seperti kuersetin, kaempferol, dan vicenin-2, yang berperan dalam proses penyembuhan luka. Selain itu, senyawa ini dapat meningkatkan penyembuhan luka dengan kondisi patologi seperti diabetes, imunokompromis dan infeksi persisten.

Keywords:

Moringa oleifera Lim.;
 pathological wound;
 phytochemical;
 wound healing;
 biological activity

INTRODUCTION

Skin is the multi-function and the largest organ in the human body. One of those functions is the first-line protector against pathogens, toxins, and trauma. If trauma or injury happens, the skin also play role in the wound healing mechanism. If the integrity of the skin is damaged or loss caused by injury or disease, it could lead to morbidity or even death.¹The Process of wound healing is very dynamic and complex, as a response to injury, cells in the skin will be activated to promote wound healing, which also attracts many other cells and substances from other parts of the body.²

The abnormalities of wound healing refer to wound scars or chronic wounds. Lots of patients develop wound scars after burns, trauma, or surgery annually worldwide. Patients with scars were reported to have decreased quality of life, physical status, and psychological health.³ Delayed chronic wound healing is one of the major biomedical and economic burdens for the global healthcare system.⁴ Nowadays, healing wound healing is still a challenging clinical problem. To have proper and efficient management in wound is crucial.⁵

Currently, existing wound management such as antimicrobial agents, modern dressings, maggots, surgical treatment, tissue sealant & platelet gel, skin substitutes, cytokines & growth factors, and recombinant hormones/enzymes cost a lot of money and are not yet available in some developing countries.^{6,7} So that currently, the majority of the trend is back to using herbal products in addition to adopting a more natural way of life.

One of the most biodiverse regions on Earth is Southeast Asia region. Even though the region occupies just a small percent of the Earth's surface, it has the highest global diversity for plant, animal, and marine species.⁸ The trend of using

natural products is increasing in most Southeast Asian countries.⁹ According to the National Agency of Drug and Food Control (NADFC) of Republic of Indonesia, many natural substances have been registered for their medical use officially; the bigger remainder is used traditionally.¹⁰

Moringa oleifera is a great value plant that grows in many tropical and subtropical regions. *Moringa oleifera* is usually known as 'horseradish tree' or 'drumstick tree'. *Moringa oleifera* is also known in various regions in Indonesia under different names such as kelor (Java, Sunda, Bali, Lampung), maronggih (Madura), moltong (Flores), keloero (Bugis), ongge (Bima), and hau fo (Timur).¹¹ *Moringa oleifera* is a high-value plant that each part of it has high nutritional value and a great range of medicinal uses.^{12,13} The empirical use of *M. oleifera* in Indonesia is as food, cosmetics, and medicine. It is used both orally or topically.^{14,15} *Moringa oleifera* is very rich in vitamins, minerals, fatty acids, and phytochemical compounds like quercetin, kaempferol, and vicenin-2.^{16,17} These compounds are trusted for anti-inflammatory, antimicrobial, antioxidant, and wound healing properties. This article discussed how *M. oleifera* may accelerate the healing of a wound in pathological conditions such as diabetes, immunocompromised and persistent infections.

MATERIAL AND METHODS

We queried PubMed, Semantic Scholar, Google Scholar, and ScienceDirect database. We included the following search terms: "*Moringa oleifera*", "*Moringa oleifera* leaves", "*Moringa oleifera* seeds", "*Moringa oleifera* bark", "wound healing", "abnormal wound healing", "chronic wound." The reference lists of the included articles and the relevant links were also manually reviewed

for additional eligible articles. Studies published in English with full text available were included. The inclusion criteria for this narrative review included the studies regarding the use of *M. oleifera* for wound healing and chronic wound healing.

RESULTS

A total 49.707 articles were found based on a search on the database according to keywords. The articles were screened to evaluate duplication and then reanalyzed to ensure eligibility according to the predetermined inclusion criteria i.e. “*M. oleifera*” and “wound healing” and “chronic wound healing”. A total 61 journals that met the inclusion criteria were then reviewed.

DISCUSSION

Wound healing

The wound-healing process is a dynamic and well-regulated process of cellular, humoral, and molecular mechanisms that begins immediately after injury and may last for years.² The process consists of four partly overlapping phases, which are hemostasis, inflammation, proliferation, and remodeling.¹⁸

Hemostasis phase

The wound will cause blood leakage from damaged blood vessels and results in rapid recruitment of platelets leading to clot formation, which next acts as a temporary shield that protect the bare blood vessels from more leakage and prevent the entry of pathogens.¹⁹ This first wound-healing phase begins immediately after wounding.²⁰ Platelets will be activated so that they will be degranulated and released chemotactic and growth factors, like platelet-derived growth factor (PDGF), transforming

growth factor- β (TGF- β), epidermal growth factor (EGF), insulin-like growth factors (IGF), proteases, and vasoactive agents (serotonin, histamine). Platelet activation causes chemokines release lead to attracting inflammatory cells to the area and initiate the next phase of the healing process.²¹

Inflammation phase

The early period of vasoconstriction is usually just 10-15 min in duration and is followed by a more persistent vasodilation period that is mediated by histamine, prostaglandins, kinins, and leukotrienes. Within hours of injury, the inflammatory phase cellular aspect occurs, and it includes mast cells, macrophages, neutrophils, and lymphocytes.²¹

Immediately after injury, mast cells become activated, degranulate, and release a large number of mediators like inflammatory cytokines, vascular permeability factors, vasodilation agents, and proteases which increases the recruitment of immune cells to the site of injury.²² Damage-associated molecular patterns (DAMPs), lipid mediators, hydrogen peroxide (H_2O_2), and chemokines released by injured cells also provide signals for inflammatory cell recruitment, particularly neutrophils.²³ Neutrophils release cytokines like TNF- α , IL-6, and IL-1 β , which intensify the inflammatory response and stimulate VEGF and IL-8 for an adequate repair response.²

The wound induces macrophages accumulation in the first 24 – 48 hours at the site of injury. In the wound healing early stages, macrophages are pro-inflammatory and microbicidal, expressing TNF- α , IL-6, and IL-1 β .²³ Macrophages are also responsible for clearing and inducing apoptotic cells (including neutrophils), thus paving the way for inflammation resolution. As macrophages clear these apoptotic

cells, they go through a phenotypic transition to a regenerative state that stimulates keratinocytes, fibroblasts, and angiogenesis to promote the regeneration of tissue. In this way, the transition to a proliferative healing phase is promoted by macrophages.²⁰

Proliferation phase

In the proliferation phase (about three to ten days after injury) the healing process's main focus is on the wound surface closure, granulation tissue formation, and vascular tissue restoration. Because of that, besides local immigration of fibroblasts along the fibrin tissue and the initiation of re-epithelialization from the wound margins, angiogenesis, and neovascularization are enabled by the growing capillaries.^{2,24}

At the end of the inflammatory phase, angiogenesis occurs. Angiogenesis involves proliferation, migration, and branching of endothelial cell to form new blood vessels. While new blood vessels arise, resident fibroblasts proliferate and invade the clot to form contractile granulation tissue. The dividing fibroblasts store the ECM and shift the microenvironment of a wound from an inflammatory state to a regenerative state. In this phase, many fibroblasts differentiate into myofibroblasts, retracting the wound margins together.²³ Myofibroblasts are known to play a central role in sealing wound tissue, through their capability to generate strong contractile forces.²⁵ About four days after wounding, myofibroblasts appear in the wound. Myofibroblasts

exert their contractile forces through focal adhesion contacts that connect the intracellular cytoskeleton to the ECM.²⁶

Remodeling phase

As the wound healing final phase, the remodeling phase is responsible for new epithelium development and the formation of mature scar tissue. The remodeling phase begins two to three weeks after the onset of injury and can last up to one to two years, or sometimes for a longer period of time. The remodeling phase aims are reorganizing and maintaining a balance between degradation and synthesis, leading to the healing of the wound with a "normal" tissue structure. The final wound strength obtained depends on the localization of the repair and its duration, but the tissue's original strength may never be regained.^{5,27}

The remodeling phase consists of neovascularization regression and periodic deposition into the ECM and reconstitution of granulation tissue into scar tissue. Granulation tissue mainly consists of collagen type III, which is partially replaced by the stronger collagen type I as wound remodeling progresses.²³ As the wound heals, the density of fibroblasts and macrophages is progressively reduced by apoptosis. Over time, capillary growth stops, blood flow to the area decreases and metabolic activity at the wound site decreases. The final result is the scar that fully matured with reduced cell and blood vessel numbers and a high tensile strength tissue.⁵

TABLE 1. Physiological wound healing phases²⁸

Wound healing phase	Histological event changes	Duration
Hemostasis	Vasoconstriction, platelet aggregation, clot formation, vasoactive agents, glycoprotein, coagulation	Minutes to hours
Inflammation	Vasodilation, neutrophils, macrophages, lymphocytes, mast cells, chemokines, growth factors, interleukins	Hours to days
Proliferation	Fibroblasts, collagen type III, granulation tissue, reepithelization, keratinocytes, growth factors, cytokines, neovascularization, endothelial cells, fibronectin, glycosaminoglycans, proteoglycans, hyaluronic acid, myofibroblasts, α -smooth muscle actin, contraction	Days to weeks
Remodeling	Neovascularization regression, reorganization of extracellular matrix, collagen fibril crosslinking, collagen type III lysis, collagen type I synthesis, apoptosis, decreased number of cells, tensile strength, scar maturation	Weeks to years

Abnormal wound healing

The natural consequence of large or deep wounds in adult mammals is the formation of scars. There is a scar formation spectrum, with scarless regeneration on one end, “normal” scar formation in the center, and pathological formation of scar, including hypertrophic scar and keloid, on the other end. Scar formation is determined by the proliferative and remodeling phase of wound healing.²⁹ Abnormal scar formation is exacerbated when the inflammation response is excessive.³⁰ The anti-inflammatory cytokine IL-10 decreases scarring, but the pro-inflammatory cytokines IL-6 and IL-8 have the opposite effect on the scar tissue response. Superficial injuries that do not reach the reticular dermis never cause keloids and hypertrophic scars. This suggests that pathological scars are caused by wounds in this skin layer and aberrant wound healing within them, which is characterized by persistent inflammation and histologically localized.³¹ A scar can have disturbing physical, aesthetic, functional, psychological, and social status so modalities are needed for prevention.³²

In addition to scar formation, when wound healing does not proceed

normally, chronic wounds will develop. These chronic wounds can be caused by underlying pathological conditions such as diabetes, abnormal immune function (immunosuppressive drugs), and persistent infections.³³ Diabetes delays the healing process because it impairs each phase of wound healing i.e. haemostasis, inflammation, proliferation, and remodeling phase. Diabetic wounds exhibit a persistent inflammatory phase associated with an impediment in the formation of mature granulation tissue and a reduction in wound tensile strength.³⁴ High blood sugar causes sustained production of pro-inflammatory cytokines, impaired macrophage and neutrophil function, imbalance in extracellular matrix regulation, impaired keratinocytes and fibroblast migration and proliferation, and impaired production of healing-associated factors like impaired growth factor production. In addition, high blood sugar levels cause a decrease in nitric oxide synthetase activity so that nitric oxide production decreases as a result, reactive oxygen species increases affect vasoconstriction, impaire platelet function and angiogenesis, and prolong inflammation.^{34,35} It takes a modality that can overcome these.

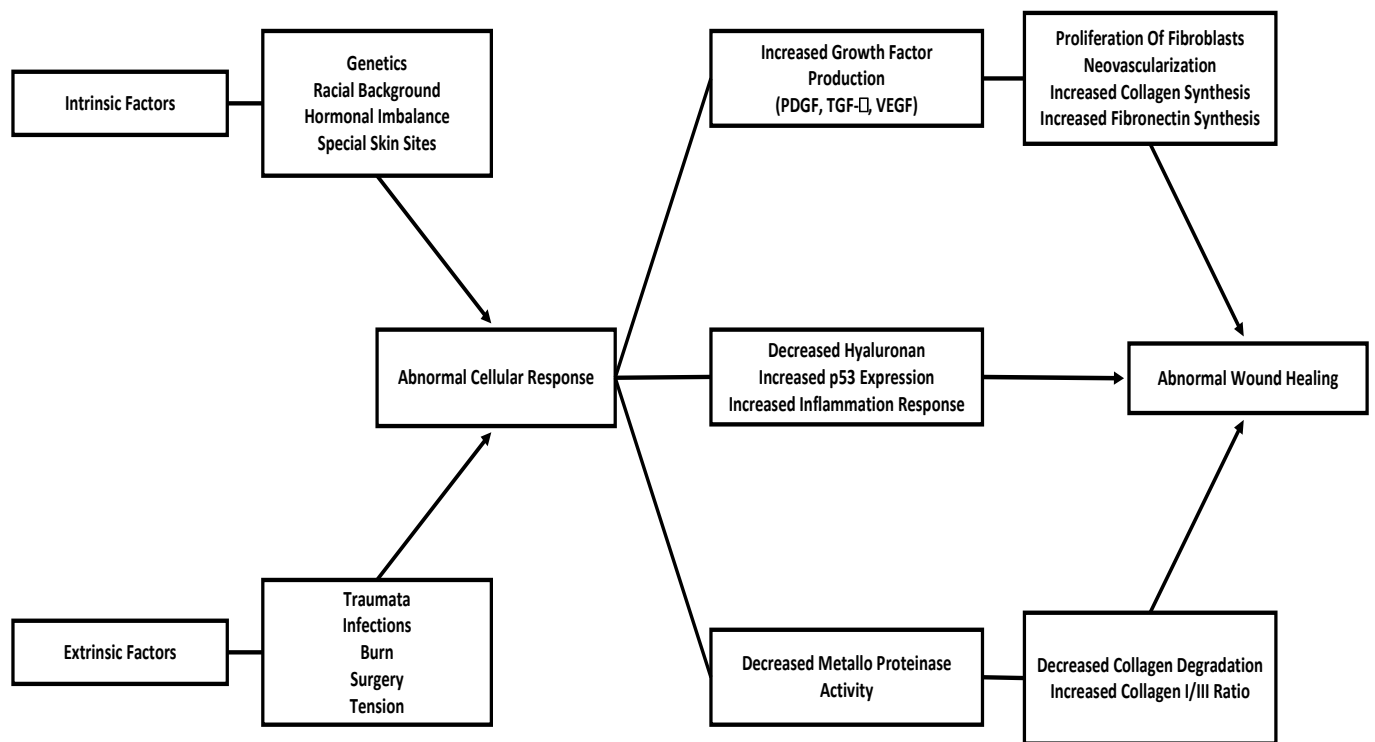


FIGURE 1. Pathogenesis of abnormal wound healing³⁶

***Moringa oleifera* compounds in promoting wound healing process**

Moringa oleifera is a cruciferous plant that belongs to the Moringaceae family. It is usually named horseradish tree or thigh tree by locals and is popular as a staple food in many parts of the world. *Moringa oleifera* is consumed not only for its high nutritional value but also for its abundant medical benefits. It is rich in proteins, minerals, β-carotene, ascorbic acid, tocopherol, polyphenols, and flavonoids which serve as a good source of natural antioxidants. Recently, it was reported to enhance various biological functions including anti-inflammatory, antimicrobial, and wound-healing properties.^{37,38}

Methanol and aqueous extracts of roots and bark, methanolic extract of leaves and flowers, and ethanolic seeds extract of *M. oleifera* have anti-inflammatory activity. *In vitro* studies of hot water infusion of flowers, leaves, roots, seeds, and stems or bark of *Moringa*

show anti-inflammatory activity. *Moringa oleifera* leaves, roots, bark, and seeds also exhibit antimicrobial activity against bacteria and fungi.³⁹

Rate of wound healing in abrasion and excision wounds in *in vivo* study was highly increased with 0.5% *M. oleifera* leaves aqueous extract film dressing. This can be related to (1) the rapid release of bioactive compounds in a 0.5% the aqueous extract film dressing to promote wound contraction (increase collagen deposition and composition by increasing COL1α1 expression), (2) the reduction of inflammatory phase after the rapid transition to the process of epidermal regeneration (upregulation of VEGF, IL-6, TNF-α) and (3) its ability to form a protective gel on the bed of wound against damage from external after absorption of exudate.⁴⁰

Moringa oleifera leaves extract per oral (gavage) has contributed to a glycemic reduction in diabetic rats lead to improv the wound-healing process.⁴¹ *Moringa oleifera* -treated

wounds showed a significant increase in fibroblast growth and proliferation, as well as faster fibroblasts migration in rats. Furthermore, the wounds treated with *M. oleifera* extract showed increased new collagen formation and collagen deposition into the wound area.⁴² The *M. oleifera* is known to contain phytochemical compounds such as flavonoids, tannins, saponins, and other phenolic compounds that have antimicrobial activity so that they can play a role in accelerating wound healing. Gothai *et al.*⁴³ reported that *M. oleifera* ethyl acetate (EtOAc) fraction at the 12.5 and 25 µg/mL concentration promotes cell proliferation and migration of normal human dermal fibroblasts.

Bioactive compounds of *M. oleifera* extract that may enhance wound healing are quercetin and kaempferol in the crude extract of methanol, and the flavone compound C-glycoside vicenin-2 in the aqueous fraction. Quercetin, vicenin-2, and kaempferol were detected in the aqueous extract of *M. oleifera* leaves to have an anti-inflammatory effect in an *in vitro* study so which may accelerate wound healing.⁴⁴ Vicenin-2 (VCN-2) is a bioactive compound and flavonoid glycoside from a subgroup of phenolics which is known as apigenin-6,8-di-C-β-d-glucopyranoside. It has been reported to possess prospective antidiabetic, antioxidant, and anti-inflammatory properties and enhance cell proliferation and migration effect.⁴⁵

Flavonoids are able to increase the growth factors needed for the process of wound healing, like EGF, TGF-α, TGF-β, PDGF, VEGF, and FGF so have faster wound healing. These benefits can accelerate the transition from the inflammatory phase to the proliferative phase so that wound healing is faster than the physiological process.¹⁶ Muhammad *et al.* stated that vicenin-2, the bioactive compound in *M. oleifera* leaves which responsible for the potent effects of cell proliferation and migration. They also

reported that *M. oleifera* leaves extract which contains vicenin-2 stimulates tissue cell proliferation, thereby reducing wound size in *in vivo* study. This extract also caused the activity of inflammatory mediators TNF-α, IL-1β, IL-6, iNOS, and COX-2 decreased and angiogenesis activity increased thereby reducing the time required for the process of wound healing.¹⁷ Vicenin-2 reduces the expression of anti-HIF1α and MMP proteins so it is very important for tissue granulation, angiogenesis formation, and re-epithelialization during the process of wound healing.⁴⁶ Tan *et al.*⁴⁵ demonstrated that both TGF-β and VEGF expression of Human Dermal Fibroblast cells was enhanced in response to treatment with vicenin-2. During the process of wound healing, VEGF induces angiogenesis via endotel proliferation and migration while TGF-β triggers remodeling and fibrogenesis by development and differentiation.⁴⁵ In the presence of flavonoids, the expression of biomarkers such as TGF-β and VEGF is increased which in turn accelerates wound healing.⁴⁷

Quercetin is a kind of polyhydroxy flavonoid, which is frequently found in flowers, leaves, and fruits of various plants. Quercetin inhibits inflammatory reactions via modulating macrophage polarization switching from M1 to M2 phenotype so that prolong inflammatory doesn't occur.⁴⁸ Quercetin has pharmacological effects including antioxidant, anti-inflammatory, angiogenic, antibacterial, immunomodulatory, increased myofibroblast activity, and proliferation of epithelial cells and fibroblasts. These properties make quercetin a promised wound-healing agent. Treatment with quercetin accelerates wound healing through (i) rapid wound contraction, (ii) controlled modulation of pro-inflammatory cytokines (TNF-α) and anti-inflammatory (IL-10), (iii) increased neovascularization via increased VEGF

and TGF- β expression, (iv) increased antioxidant status at the wound site, and (v) increased fibroblast proliferation with marked collagen deposition and increased myofibroblast formation. Expression of growth factors involved in angiogenesis, collagen synthesis, and extracellular matrix (ECM) such as VEGF and TGF- β 1 increased on days 3 and 7, respectively.⁴⁹ Furthermore, it has provided a mechanism that enhances wound healing; open excision wounds in adult mice given topical 0.1% quercetin (*in vivo* study) showed accelerated wound closure results in treated mice, whereas the level of TNF- α decreased with better re-epithelization, more regular deposition of collagen, and VEGF and TGF- β 1 upregulated.⁵⁰ The active compound, kaempferol and its glycosides promote wound healing through keratinocyte cell migration. Effects on keratinocyte migration of kaempferol via FAK/Akt activation and enhances cellular filopodia and lamellipodia formation via activation of Rac1.⁵¹ Quercetin and kaempferol are flavonoids that have a similar chemical structure, which is why both of compounds have similar biological activities also, and can work synergically to maintain the function of the endothelium of blood vessel for the promotion of angiogenesis and inhibits hypoxia.⁵²

Moringa oleifera also contains lauric acid, myristic acid, palmitic acid, arachidonic acid, and oleic acid that triggers fibroblasts to induce various growth factors in the wound, in particular TGF- β 1 and VEGF. The *M.*

oleifera leaves EtOAc fraction can be a novel candidate for dermal wound healing because of the effectiveness of its antibacterial properties against various pathogens, especially skin infection-causing pathogens. Phenolic compounds in the *M. oleifera* leaves EtOAc fraction have antioxidant activity that acts as hydrogen donors or reducing agents, which improves regeneration and organization of the new tissue in wound healing.⁵³ *Moringa* flowers and seeds also have antioxidant and anti-inflammatory activities due to their compounds such as ascorbic acid, carotenoids, tannins, alkaloids, glycosides, flavonoids and phenolic compounds kaempferol, quercetin, and the unique combination of fatty acids in the flower extract.^{38,54}

In an *in vitro* study, a combination of *M. oleifera* and *Aloe vera* containing quercetin to treat wounds, showed the highest anti-inflammatory effect and quercetin treatment with higher phenolic content was a modality with higher anti-inflammatory activity.⁵⁵ The anti-inflammatory effect through the inhibitory activity of NF- κ B, inhibits the secretion of nitric oxide and pro-inflammatory markers like prostaglandin E2, TNF- α , and IL-6, at the same time induce anti-inflammatory cytokines production like IL-10 in a dose-dependent manner. Quercetin also showed antibacterial activities by inhibit of *Staphylococcus aureus*, *S. epidermidis*, and *S. pyogenes* growth. This makes it a suitable wound treatment formulation candidate.⁵⁶

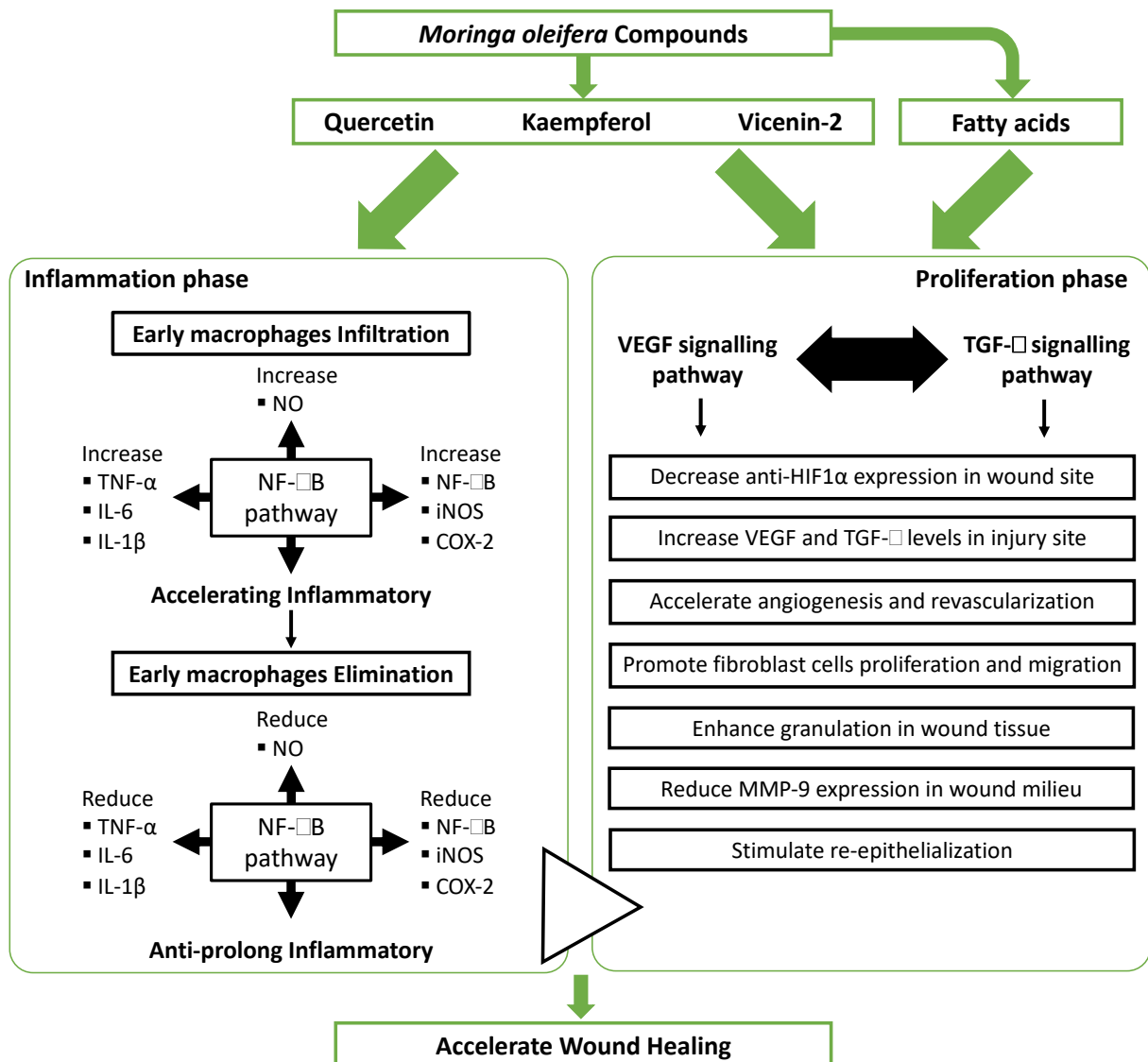


FIGURE 2. Signaling pathways of *Moringa* compounds to accelerate wound healing process⁴⁶

Effect of *M. oleifera* extract on chronic wounds

Chronic wounds are associated with microorganisms due to the bacteria colonization on the wounds within 48 h after injury. These may cause an infection that affects the wound-healing process by prolonging the inflammatory phase. The antibacterial properties exhibited by an aqueous fraction of *M.*

oleifera may be linked to the presence of some phytochemical compounds, such as alkaloids, triterpenoids, tannins, and flavonoids. These compounds promote the wound-healing process mainly due to their astringent and antimicrobial properties, which are responsible for wound contraction and increased rate of epithelialization. The aqueous fraction of *M. oleifera* strongly inhibiting the *S. aureus*, *P. aeruginosa*, and *E. coli* growth

suggests its ability to facilitate wound healing through antibacterial action.¹⁶

Topical application of aqueous fraction of *M. oleifera* reduced wound size and improved contraction rate in diabetic rats. An increase of collagen deposition and better alignment and maturation of wound tissue were observed. Downregulation of proinflammatory cytokines (IL-1 β , IL-6, and TNF- α), iNOS and COX 2, and an increase of VEGF expression that promotes angiogenesis were also reported.¹⁶ Administration of *M. oleifera* extracts on diabetic rats for 21 demonstrated significant rejuvenation of pancreatic islets, reduced serum glucose in addition to increased serum insulin level coupled with improved antioxidant status by decreasing oxidative stress/lipid peroxidation. *Moringa oleifera* significantly suppressed levels of NF- κ B in diabetic rats by enhances cellular antioxidant defense potential, therefore able to minimize abnormal cell proliferation.⁵⁷ Healing impairment in diabetic ulcers has a number of physiological causes including diminished fibroblast proliferation and angiogenesis. The *M. oleifera* ethyl acetate fraction supported the wound healing activity by promoting the proliferation and migration of fibroblast cells and neovascularization.⁵³

Moringa oleifera contains amino acids, fatty acids, vitamins, and trace elements that are all important in cell-mediated immune responses. Fatty acids, vitamin D, and trace elements that not only facilitate the proliferation and maturation of neutrophils, but also the secretion of cytokines that enhance neutrophil migration and adhesion. This suggests that the presence of these compounds in *M. oleifera* extract may be useful in protecting the body. Vitamins A, C, K, and amino acids present in *M. oleifera* extract can be attributed to the

ability to activate lymphocytes and their accessory cell types leading to increased antibody production in previously immunosuppressed animals thereby enhancing cell-mediated immunity. Therefore, plant extracts can be used when the immune system is compromised to enhance cell-mediated immune responses as the extracts enhance the phagocytic activity of neutrophils and increase antibody production.⁵⁸

Moringa oleifera seeds oil and its principal compound oleic acid increased tissue collagen during the chronic wound healing process, and reverted contractile reduction of myofibroblasts in the amelioration of immunosuppression and diabetes. It also accelerates the inflammatory phase of regular injury repair, increases TNF- α concentration and neutrophil numbers in the area of injury, and reduces IL-1, IL-6, and MIP-3 α concentrations. It is responsible for efficiently accelerating inflammation, thus, appropriately stimulating fibroblast activity, wound myofibroblast contraction, and matrix deposition in chronic wound healing in immunosuppressed and diabetic mice.⁵⁹ Water-soluble lectins from *M. oleifera* seeds promoted immunomodulation in human peripheral blood mononuclear cells that induced a potential wound healing profile through activation of CD8+ T lymphocytes.⁶⁰

The aqueous extract of *M. oleifera* bark increases the amount of hydroxyproline (a direct estimate of collagen synthesis) and also opposes the action of dexamethasone to some extent on collagen synthesis, maturation, deposition, epithelialization period, and hydroxyproline content. Thus, it has the potential to counteract the anti-healing effects of steroids in patients that receive steroid therapy.⁶¹

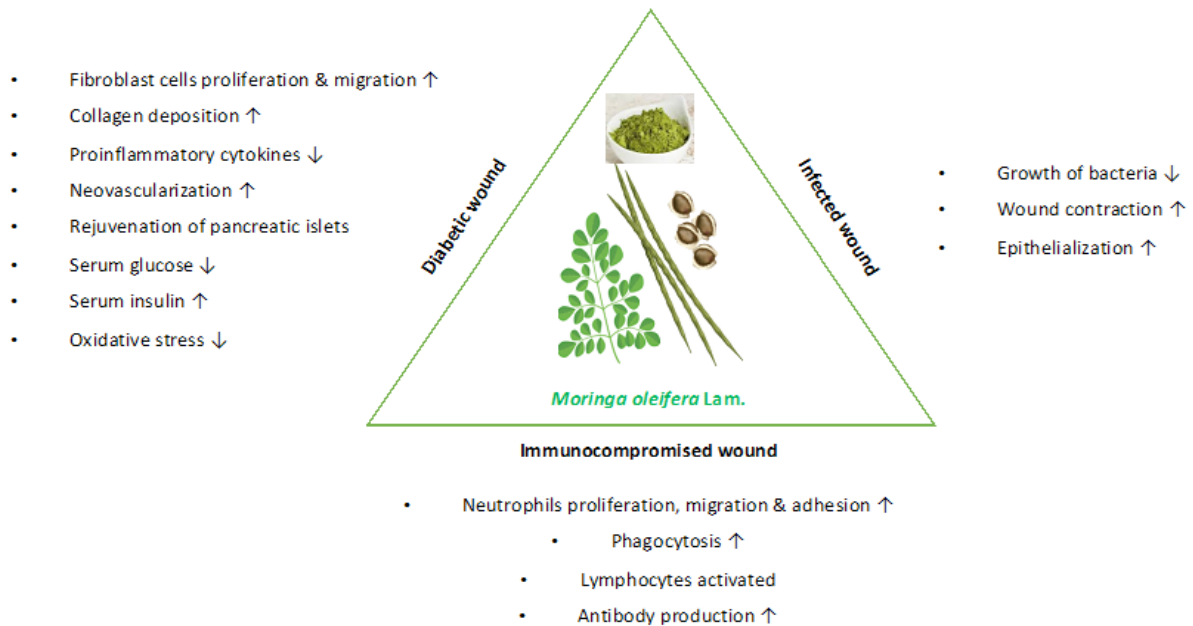


FIGURE 3. Effects of *M. oleifera* leaves in pathological wounds

CONCLUSION

In conclusion, *M. oleifera* extract which contains vitamins, proteins, minerals, fatty acids, and phytochemical compounds like quercetin, kaempferol, and vicenin-2 can accelerate wound healing by reducing the time of the inflammatory phase and the transition time to regeneration, proliferation and migration phase of epidermal due to many growth factors that contribute to cell proliferation, triggering collagen and angiogenesis formation. *Moringa*

oleifera extract has activity in enhancing wound healing and it may be one of the modalities used in chronic wounds on patients with diabetes mellitus, immunocompromised and persistent infections. Further clinical studies are needed to prove the potential effects of *M. oleifera* as wound healing agents.

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