ISSN: 1672 - 6553

JOURNAL OF DYNAMICS AND CONTROL

VOLUME 10 ISSUE 07: P27-46

EXPERIMENTAL AND MOLECULAR INSIGHTS INTO THE WOUND HEALING POTENTIAL OF PLANT-BASED SAPONINS: A COMPREHENSIVE REVIEW

Abhinash Saini, Vinod kumar, Sonia, Komal, Maninder Lamba, Rahul Singh

Department of Pharmacy, School of Healthcare and Allied Sciences, G.D. Goenka University, Sohna-Gurugram Road, Sohna, Haryana - 122103, India

JOURNAL OF DYNAMICS AND CONTROL
https://doi.org/10.71058/jodac.v10i07003

EXPERIMENTAL AND MOLECULAR INSIGHTS INTO THE WOUND HEALING POTENTIAL OF PLANT-BASED SAPONINS: A COMPREHENSIVE REVIEW

Abhinash Saini*, Vinod kumar, Sonia, Komal, Maninder Lamba, Rahul Singh
Department of Pharmacy, School of Healthcare and Allied Sciences,
G.D. Goenka University, Sohna-Gurugram Road, Sohna, Haryana - 122103, India
Corresponding Author: sainimonu59327@gmail.com

Abstract: *The process of wound healing is a multidimensional and highly regulated biological process with mechanisms of control of inflammation, cell growth, angiogenesis, and remodelling of the extracellular matrix. Although the tradition of wound care advanced, the control of acute and chronic wounds is still difficult because of high expenses, side effects, and low effectiveness of single-target treatment. This has promoted the growing interest in alternative therapeutic agents in terms of plant-derived bioactive compounds. Saponins among them have also received much interest due to their varied pharmacological features and conventional exploitation in the treatment of wounds.*

This current review will study experimental and molecular data based on the potential of saponins exerted by plants in healing wounds, in a comprehensive manner. A databases search was performed on PubMed, Scopus, ScienceDirect, and Google Scholar databases and included all publications published from 2014 to 2024. An inclusion was made of both in-vivo and in-vitro experimental research assessing wound healing activity and the underlying molecular mechanisms. All these studies indicate that saponins stimulate wound contraction, epithelialization, collagen production, and angiogenesis. At the molecular level, saponins regulate the major mediators of inflammation, enhance the antioxidant defense mechanisms, control the expression of growth factors and contribute to the extracellular matrix restructuring.

In general, the results elicit the multi-target therapeutic capability of plant-based saponin in healing wounds. Despite the promise, they still need to be finally clinically validated, standardized, and further formulation techniques in order to be converted into useful wound care treatments. This review presents a scientifically unified foundation of further research and clinical development of the wound healing agents based on saponin.

Keywords: *Angiogenesis; Molecular mechanisms; Plant-based saponins; Tissue regeneration; Wound healing*

1. Introduction

The process of wound healing is a very complicated and well-coordinated biological process that reinstates the structural and functional integrity of the damaged tissue [1]. Wound management is a significant clinical problem that is experienced by people across the globe despite the intensive session in medical science. Both acute and chronic wounds have significant economic cost implications on healthcare systems as well as impact the quality of life of the patients [31]. The increasing incidence of wound that cannot heal has increased the urge to consider the implementation of safer and cost-effective and biologically active therapeutic options [32]. In this regard, bioactive compounds of plant origin and especially

https://doi.org/10.71058/jodac.v10i07003

saponins have attracted growing interest over the last few years due to their various pharmacological and conventional application in the treatment of wounds.

1.1 Global Burden of Acute and Chronic Wounds

Wounds pose an important health issue in the society with millions of people worldwide getting them every year. Acute wounds such as surgery cuts, burns, and traumatic wounds are usually healed in a progressive stage as long as they are well-attended. Conversely, chronic wounds that include diabetic foot ulcers, pressure ulcers, venous leg ulcers, among others, do not proceed through the standard phases of healing and can be incompletely extended over months/years [2]. Chronic wounding is on the increase because of aging, escalating cases of diabetes, overweight and vascular illnesses [33]. The wounds are related to the long hospital stay, the risk of infection, the amputation of a limb, and death, and it is necessary to develop more effective treatment options.

1.2 Limitations of Current Wound Healing Therapies

The classic wound healing solutions are antiseptics, antibiotics, anti-inflammatory medications, growth factors and high-tech wound dressings [3]. Although these methods have contributed to a better wound care outcome, they are usually characterized by various constraints. Antimicrobial resistance, slow healing, and systemic side effects can result during the long-term use of antibiotics [34]. Synthetic growth factors are also expensive and they can show low stability and bioavailability. Also, numerous conventional treatment strategies focus on the one-pathway treatment, when wound healing is a multidimensional process that includes inflammation, oxidative stress, angiogenesis, and extracellular matrix remodelling [35]. These shortcomings highlight the necessity of having alternative therapy with the capacity to target more than one biological target at a time.

1.3 Role of Medicinal Plants in Wound Management

The traditional systems of medicine have been using medicinal plants to treat wounds and skin ailments in centuries. Plant-based therapies have been appreciated by their availability, low costs, and wide range of biological properties. Many plant extracts have been shown to have wound healing properties based on the effect of anti-inflammatory, antioxidant, antimicrobial, and collagen-stimulating [4]. Compared with synthetic drugs, phytochemicals tend to work together in order to regulate various wound healing stages [36]. This is a multi-targeted activity, which thrives medicinal plants as potential source of new wound healing agents.

1.4 Overview of Saponins and Their Pharmacological Importance

Saponins are naturally available glycosides that are greatly spread in the medicinal plants. They are structurally composed of hydrophobic aglycone to which one or more sugar moieties have been attached, which reflects in their variety of biologically active processes. [5]**.** Saponins was reported to have anti-inflammatory, antioxidant, antimicrobial, immunomodulatory and angiogenic activities [37]. According to experiential research, saponins may benefit fibroblast proliferation and collagen production, induce neovascularization, and control several major molecular mediators of tissue repair. Such properties make saponins promising bioactive compounds to be used in wound healing.

https://doi.org/10.71058/jodac.v10i07003

1.5 Research Gap and Rationale of the Review

In spite of a handful of experimental studies done to examine the wound healing activity of saponin rich plant extracts, the existing information is disjointed. In the majority of the reviews, medicinal plants or phytochemicals have gotten a general overview without the rigorous examination of the experimental models and molecular mechanisms involved in saponin [6]. There is no detailed synthesis of in-vitro, in-vivo and molecular evidence. This gap needs to be bridged so that the therapeutic potential of plant-based saponins can be better comprehended and that it can be incorporated into translation between the experimental studies and the clinical practice.

1.6 Objective of the Review

The main aim of this review is to critically evaluate experimental and molecular data that PD-purified saponins in plants have wound healing potential. This review will be based on summing up their impact on various wounds healing stages, mentioning the underlying molecular mechanisms, weighing their merits on conventional therapies, and stating contemporary limitations and research directions [7]. This review aims to offer some scientific foundation on the development of saponin based wound healing therapeutics by synthesizing the evidence available.

2. Methodology of Literature Search

In order to determine the potential of plant-based saponins in wound healing, a systematic and organized literature review was carried out to obtain available experimental and molecular research on the topic [8]. The design of the methodology was carried out based on the common principles of writing review articles so that the work would be transparent, reproducible, and would cover all the literature available.

2.1 Databases Used

To give a comprehensive literature search, the following electronic databases have been used: PubMed, Scopus, ScienceDirect, and Google Scholar. The chosen of these databases was aimed at a broad coverage of the biomedical, pharmacological, and interdisciplinary research pertaining to wound healing and the plant-derived bioactive compounds [9]. All articles online that match the specified period of interest were downloaded out of each database and moved to the next phase of screening and processing.

2.2 Search Strategy

Relevant studies were retrieved by using a mixture of controlled vocabulary words and free-text keywords. The main search terms were these; wound healing, saponins, plant-based saponins, medicinal plants, cutaneous wound, skin regeneration and molecular mechanisms. Search strategy was refined using the such operators like AND and OR. The combinations used as representative search strings comprise of wound healing AND saponins, plant saponins AND skin repair, and saponins AND molecular mechanisms AND wound healing [10]. Only magazines that were written in English were in the search.

https://doi.org/10.71058/jodac.v10i07003

2.3 Inclusion Criteria

The studies were incorporated in the review according to the following criterion:

(i) original research studies that are published in peer-reviewed journals;

(ii) researches done on in-vitro or in-vivo experimental wound models;

(iii) Studies which test the wound healing response of plant-derived saponins or saponin-containing extracts;

(iv) those studies whose outcomes are on a molecular, biochemical or histopathological outcome under wound healing; and

(v) papers that are published between the years 2014 and 2024.

2.4 Exclusion Criteria

The studies were also eliminated when they satisfied the following criteria:

(i) articles or other non-peer-reviewed works of opinion, editorials or editorial opinion articles;

(ii) case reports, conference abstracts, theses of revision articles;

(iii) literature that has not been experimentally validated to find wound healing activity;

(iv) the articles that are not in English language;

(v) research of inadequate methodological information or outcome measure.

https://doi.org/10.71058/jodac.v10i07003

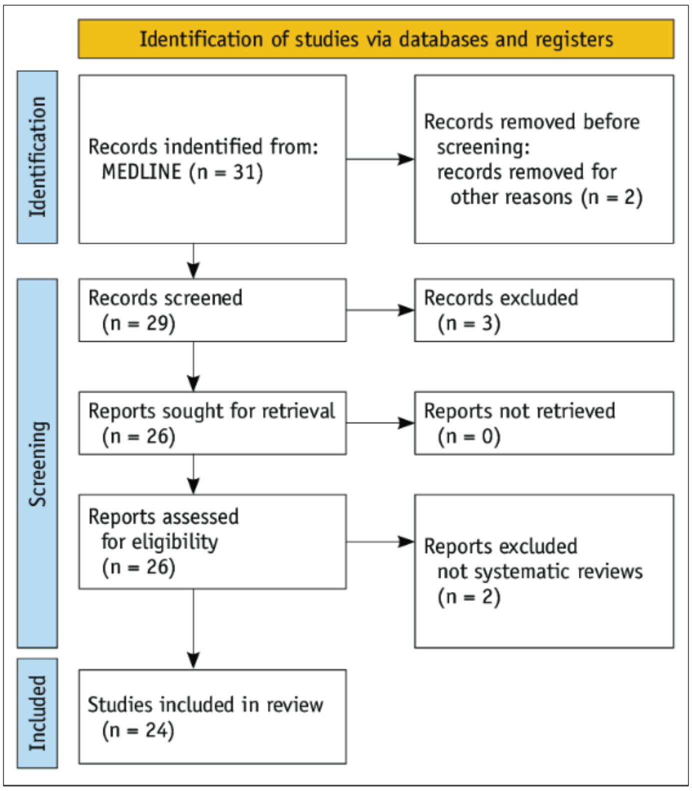


Figure 1: PRISMA Flow Diagram for Study Selection

The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 372, n=71.https://doi.org/10.1136/bmj.n71

Figure 1 illustrates the stepwise process followed for the identification, screening, eligibility assessment, and final inclusion of studies evaluating the wound healing potential of plant based saponins. The diagram is structured in accordance with PRISMA guidelines to ensure transparency and reproducibility of the literature selection process.

3. Overview of Wound Healing Physiology

Wound healing is a biological process, which is dynamic and very coordinated and which regains tissue integrity after injury. It is composed of stages of overlapping that are controlled by cellular interactions, signaling molecules and extracellular matrix components [11]. Any deviation of such tightly regulated events is likely to cause delays in healing and cause chronic wound formation. The biological premises of wound healing are instrumental to determining the therapeutic values of bioactive substances like saponins that are found in plants [38].

3.1 Hemostasis

The instant reaction to injury to tissues is the process of hemostasis which starts minutes after a wound has been formed[12]. The main aim of this stage is to arrest bleeding and provisional wound matrix. After a vascular damage, a vasoconstriction takes place, and platelets clotting to the damage point to create a fibrin clot takes place [39]. This clot does not only inhibit excessive blood loss but also has a temporary scaffold formation of the cell migration. Several platelet-derived growth factors such as platelet-derived growth factor and transforming growth

https://doi.org/10.71058/jodac.v10i07003

factor beta are released by the platelets and trigger the later inflammatory and repairing processes.

3.2 Inflammation

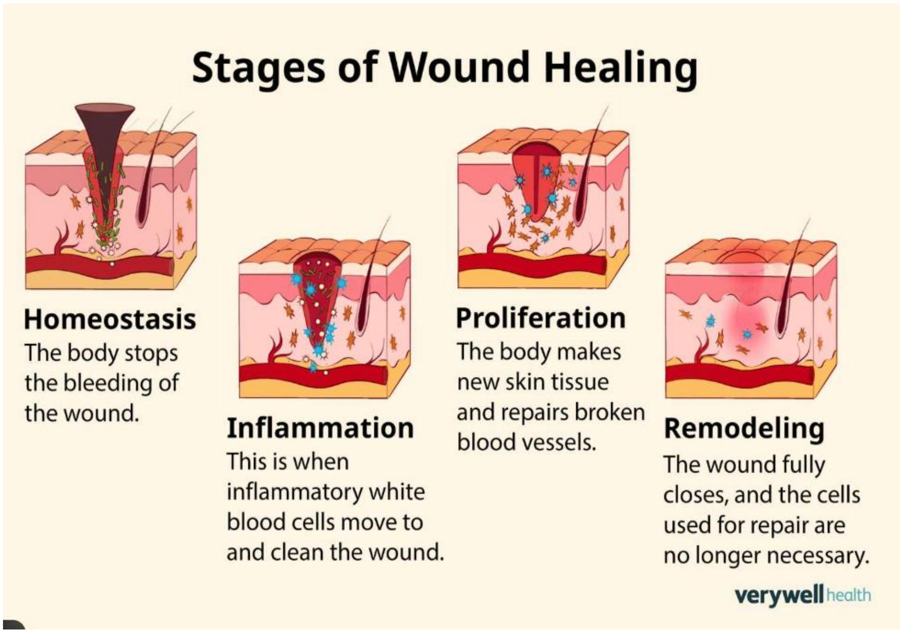
Inflammatory stage comes after the hemostasis, and it is marked by attracting immune cells to the wound. The initial cells to enter the wound are the neutrophils which are used in the removal of bacteria and cellular debris [13]. The neutrophils are then replaced by the macrophage which is found to be central in orchestrating the wound repair [40]. Such cells secrete cytokines, chemokines, and growth factors which control inflammation, trigger angiogenesis and trigger fibroblasts and keratinocytes. Although inflammation is vital to normal healing, its persistence, and excessive plate could inhibit tissue restoring and lead to the formation of chronic wounds.

3.3 Proliferation

There is active tissue growth and wound bed remediation that characterizes the proliferative stage. Fibroblasts move into the wound area and produce parts of the extra cellular matrix and especially collagen [41]. At the same time, keratinocytes increase in number and move over the wound, to re-epithelialize the wound. The Angiogenesis process also takes place at this stage and new blood vessels are formed that supply the regenerating tissue with oxygen and nutrients [42]. The processes of granulation tissue, re-epithelialization, and neovascularization are interim issues that are essential in the achievement of successful wound closure.

3.4 Remodeling

The last phase of wound healing is called remodeling or the maturation stage and this stage may take several weeks to months [14]. In this stage, there is reorganization and substitution of collagen fibres into more organized and stronger collagen to enhance tensile strength [43]. The surplus cells go through apoptosis and new blood vessels make a retreat as the tissue goes back to a close-to-normal condition [44]. Even when the healed tissue is uncommon in the strength of healthy skin, functional remodeling is required in order to provide the control of scar formation and functional recovery [45].



https://doi.org/10.71058/jodac.v10i07003

Figure 2: Schematic Representation of Phases of Wound Healing

Source: Gurtner GC, Werner S, Barrandon Y, Longaker MT. 2008. *Wound repair and regeneration.***Nature**, 453:314-321. https://doi.org/10.1038/nature07039

Figure 2 provides a schematic overview of the four overlapping phases of wound healing: hemostasis, inflammation, proliferation, and remodelling. The diagram highlights the temporal sequence of events and the key cellular and molecular processes involved in successful tissue repair.

3.5 Influence of Plant-Based Saponins on Different Phases of Wound Healing

There is experimental evidence to indicate that plant-based saponins are capable of positively impacting at various stages of the wound healing process. The anti-inflammatory and antioxidant effects of saponins occur when they are in hemostatic and inflammatory phase and are useful in check excessive immunological responses. Saponin has been found to increase fibroblast proliferation, promote collagen synthesis and angiogenesis in the proliferative stage [15]. They also have the capacity to regulate growth factor expression which facilitates re-epithelialization. In the remodelling step, saponins will aid collagen filing and extracellular remodelling which leads to a better wound toughness and lesser scarring. This multi-step, multi-objective action suggests the therapeutic promise of saponins as a good wound healing phytotransducer [46].

4. Plant-Based Saponins: Classification and Sources

Plant-based saponins represent a wide family of naturally occurring glycosides that is generally very popular in medicinal plants [16]. They are of structural diversity and have a wide spectrum of pharmacological activity that has gained a lot of attention in wound healing studies. Saponins can be widely divided based on the chemical character of their aglycone group to triterpenoid and steroidal saponins [47]. A number of medicinal plants that contain these compounds have been shown to have potential wound healing in experimental studies.

4.1 Classification of Saponins

Saponins are amphiphile molecules that consist of hydrophobic aglycone that is attached to a hydrophilic sugar chain. This special architecture renders them to be biologically active i.e., for membrane interaction, signaling pathway modulation, and regulation of inflammatory responses [17].

4.1.1 Triterpenoid Saponins

Triterpenoid saponins are compounds that have a pentacyclic triterpene structure and usually in most medicinal plants that are used as traditional medicine [18]. These antioxidants, anti-inflammatory, and tissue regenerative properties of these saponins have been utilized widely. Triterpenoid saponins are demonstrated to stimulate fibroblast proliferation, stimulate collagen deposition, stimulate angiogenesis, and epithelialization has been reported to hasten wound healing modeling. They are especially useful in the skin repair process because they have the ability to control the factors of growth and the remodeling of the extracellular matrix.

https://doi.org/10.71058/jodac.v10i07003

4.1.2 Steroidal Saponins

Saponins containing steroids have a steroid nucleus as its aglycone structure [19]. In spite of their lower concentration than the triterpenoid saponins, they have strong biological functions like immunomodulatory and anti-inflammatory effects. According to the experimental studies, steroidal saponins may be applied as an adjunct to wound healing by lowering undue inflammation, promoting granulation tissue growth, and enhancing the tensile strength of the healed tissue. Their chemical similarity to the inherent steroid molecules could help in their control over cellular signalling pathways of tissue repair.

4.2 Medicinal Plant Sources of Saponins

Multiple medicinal plants with high saponin concentration have been studied in terms of their wound healing effect. Some of the most common plants cited in the experimental studies include the following.

4.2.1 Asparagus racemosus

Asparagus racemosus is a popular remedial herb that is traditionally applied in immunomodulatory and anti-inflammatory effects [20]. It has been reported to have its saponin constituents that help in wound contraction, shortening of the wound healing time, and collagen production in experimental wound models. These are because of its antioxidant effect and tissue regeneration power.

4.2.2 Centella asiatica

Centella asiatica has been known to be used as a skin regenerative agent and also in wound healing. The plant has triterpenoid saponins which activate the growth and the production of collagen and angiogenesis of the fibroblasts. It has been proven that healed wounds treated with saponin-rich extracts of this plant get faster and better epithelialization, as well as high tensile strength [21].

4.2.3 Panax ginseng

The ginsenosides that are abundant in panax ginseng belong to the group of triterpenoid saponins that has various pharmacological properties [48]. Ginsenosides have been demonstrated to have pro-angiogenic, anti-inflammatory, and keratinocyte migratory effects in wound healing research. These measures result in quick healing of wounds and enhanced tissue healing.

4.2.4 Glycyrrhiza glabra

Glycyrrhiza glabra or licorice is a plant with glycyrrhizin and saponins constituent, which has anti-inflammatory and antioxidant action**s** [22]. The application of these saponins on wound models has demonstrated effects of repressed inflammatory infiltration of cells by these saponins, increased granulation tissue formation and collagen maturation resulting in a better wound healing process.

https://doi.org/10.71058/jodac.v10i07003

Table 1. Plant Source, Type of Saponin, Experimental Model, and Key Wound Healing Outcomes

Medicinal Plant Source	Type of Saponin	Experimental Model	Key Wound Healing Outcomes
Asparagus racemosus	Steroidal saponins	Excision and incision wound models (rats)	Accelerated wound contraction, reduced epithelialization time, increased collagen deposition, improved tensile strength
Centella asiatica	Triterpenoid saponins	Excision wound model; fibroblast proliferation assays	Enhanced fibroblast proliferation, increased collagen synthesis, improved angiogenesis, faster re-epithelialization
Panax ginseng	Triterpenoid saponins (ginsenosides)	Burn and excision wound models; keratinocyte migration assays	Increased angiogenesis, enhanced keratinocyte migration, reduced inflammation, improved granulation tissue formation
Glycyrrhiza glabra	Triterpenoid saponins (glycyrrhizin)	Excision wound model; anti-inflammatory assays	Reduced inflammatory cell infiltration, enhanced granulation tissue formation, improved collagen maturation
Aloe vera	Triterpenoid saponins	Excision and burn wound models	Faster wound contraction, enhanced epithelialization, improved histopathological architecture
Tribulus terrestris	Steroidal saponins	Incision wound model	Increased wound breaking strength, improved collagen fiber organization
Quillajasaponaria	Triterpenoid saponins	In-vitro fibroblast proliferation assays	Stimulated fibroblast growth, enhanced extracellular matrix synthesis

Table description:
This table provides an overlay of medicinal plant sources of saponins, the saponin type, wound models that were used in experiments and the significant wound healing results, such as wound contraction, epithelialization, collagen deposition histopathological results.

5. Experimental Evidence of Wound Healing Activity of Saponins

The plant-based saponins have been widely experimentally proven as have a large amount of supporting evidence on their potential in wound healing [23]. The effects of both models on various tissue repair stages have been widely tested using both in-vivo animal and in-vitro cellular assays. All these studies expressly indicate that saponins are known to improve healing

https://doi.org/10.71058/jodac.v10i07003

by increasing wound healing, tissue regeneration and altering important biological events that play a role in wound healing.

5.1 In-Vivo Experimental Studies

In-vivo wound models are also needed in the assessment of overall healing response, where it is possible to assess the tissue repair within a complex biological milieu. Plant extracts rich in saponins and purified saponins have been assayed using different standardized animal wound assays [49].

5.1.1 Excision Wound Models

The excision wound model is rather one of the most common models of wound healing. In this model, a complete thickness of skin tissue is excised and wound contraction and epithelialization is tracked up to time. Some of the studies have shown that plant-based saponins treatment greatly hastens wound contraction and shortens time to full epithelialisation [24]. It has also been shown that saponin-treated wounds have enhanced granulation tissue formation, collagen deposition and angiogenesis in supplement.

5.1.2 Incision Wound Models

Incision wound model is most widespread in determining the tensile strengths of the healed tissue[50]. The wound breaking strength is assessed after the specified period in this model where a linear incision is made and sewn. Groups treated with saponin have shown enhanced tensile performance than the controls showing enhanced collagen maturation and the maturing tissue pace integrity. These results indicate a good presence of saponins in reinforcing new skin.

5.1.3 Burn Wound Models

The models of burn wounds are applied in the investigation of the healing in extreme conditions of severe tissue damage and inflammation. As experimental evidence indicates, the use of saponins in the treatment inhibits the occurrence of inflammatory reactions, leads to better re-epithelialization, and accelerates wound healing in deep burn injuries [25]. Higher vascularization and diminished scarring have also previously been reported pointing to the prospects of saponins in the management of intricate wounds.

5.2 In-Vitro Experimental Studies

In-vitro research offers the mechanistic outcomes of the cellular actions of saponins on wound healing. The assays target major cells, which are used in the repair of tissues such as fibroblasts and the keratinocytes.

5.2.1 Fibroblast Proliferation Assays

Fibroblasts are very important in the formation of the extracellular matrix and wound contraction. The in-vitro research incorporating the use of fibroblast cell lines has shown that saponins depict specific dose-dependent stimulation of cell growth and synthesis of collagen

https://doi.org/10.71058/jodac.v10i07003

[26]. These effects have an effect of increasing the granulation tissue formation and structural support in wound repair.

Migration and scratch assays: Keratinocytes can be assayed using scratch tests and migration assays that involve the formation of a scratch within a setup, which is thereafter covered over with a cell-friendly gel.

5.2.2 Keratinocyte Migration and Scratch Assays

Keratinocytes can also be cultured by the use of scratch tests and migration assays where they are set up a scratch in a medium which is then overlaid by a gel friendly of cells.

The wound re-epithelialization relies on the migration of keratinocytes [27]. Scratch assays and migration measurements have demonstrated that the saponins stimulate the movement of the keratinocytes and gene healing in the gap of the wounds. The practice aids in the expedited healing of the epidermal layer and enhancing surface recovery.

5.3 Common Outcome Parameters Used in Studies

The experimental studies that are evaluating the wound healing activity of the saponins are usually evaluating a set of standardized outcome parameters. These are wound contraction, indicating the contraction of the area of the wound over time; epithelialization time, which is the time that it takes to cover the surface entirely; histopathological measurements where there is organization of collagen, infiltration of inflammatory cells, and their neovascularization. These parameters, when combined, allow giving the comprehensive evaluation of the healing process and therapeutic potential of saponins.

6. Molecular Mechanisms of Action of Plant-Based Saponins in Wound Healing

Plant-based saponins have wound healing effects resulting by regulating various molecular pathways involved in inflammation, oxidative stress, cell proliferation and extracellular matrix remodelling [28]. Finally, saponins regulate the interlinked signalling cascades which in combination with each other, enhance tissue healing as opposed to single-target synthetic drugs. There is an increasing body of evidence with regard to the compounds regulating key mediators that are vital in promoting efficient and balanced healing after wounds through experimental research.

6.1 Anti-Inflammatory Mechanisms

Inflammation is a key early wound healing stage but prolonged, or excessive, inflammation may slow down tissue healing and hasten the development of chronic wounds. Plant based saponins were reported to have a great level of anti-inflammatory effects that involved the regulation of pro-inflammatory cytokines and signal pathways [29]. The experimental studies have shown that saponins inhibit the tumor necrosis factor alpha, interleukin-1 beta, and interleukin-6 expression, thus decreasing the wound site inflammatory cell infiltration. Moreover, it has been found to inhibit nuclear factor kappa B signaling which results in the down regulation of inflammatory genes. Saponins aid in the regulation of immune response

https://doi.org/10.71058/jodac.v10i07003

which is necessary to proceed to the proliferative stage by suppressing inflammation in a controlled manner.

6.2 Antioxidant Activity

Oxidative stress due to the over activity of the generation of reactive oxygen species may affect wound healing by causing damage to cellular components and increasing inflammation [30]. In both in-vitro and in-vivo Saponins have been shown to be great antioxidants. These substances augment the exercise of endogenous antioxidant catalysts which incorporate superoxide dismutase, catalase, glutathione peroxidase, and lower lipid peroxidation signs. Saponins preserve fibroblasts, keratinocytes, and endothelial cells through hampering oxidative damage, hence, provides tissue regeneration with a good microenvironment.

6.3 Modulation of Growth Factors

The growth factors are highly significant towards controlling cell migration, the proliferation, the angiogenesis and the establishment of the matrix to heal the wound. Plant based saponins have also been reported to regulate the expression of major growth factors such as platelet-derived growth factor, vascular endothelial growth factor and transforming growth factor beta. Their upregulation enhances the fibroblast activation, keratinocyte migration and neovascularization. Increased angiogenesis raises oxygen and nutrient delivery to the wound site speeding up the formation of granulation tissue and epithelial regeneration.

6.4 Collagen Synthesis and Extracellular Matrix Remodeling

The growth of collagen and breaking down of the extracellular matrix is required to heal structural integrity of tissue damage. According to experimental studies, saponins enhance the level of hydroxyproline which is an indicator of improved collagen synthesis. They also mediate the presence of the matrix metalloproteinases and their inhibitors in order to maintain the controlled degradation of the matrix as well as its remodelling. Saponin-treated wounds have been found to possess improved collagen fiber organization and tensile strength of the healed tissue and have been proposed to contribute towards successful maturation and

https://doi.org/10.71058/jodac.v10i07003

remodelling of the wound matrix.

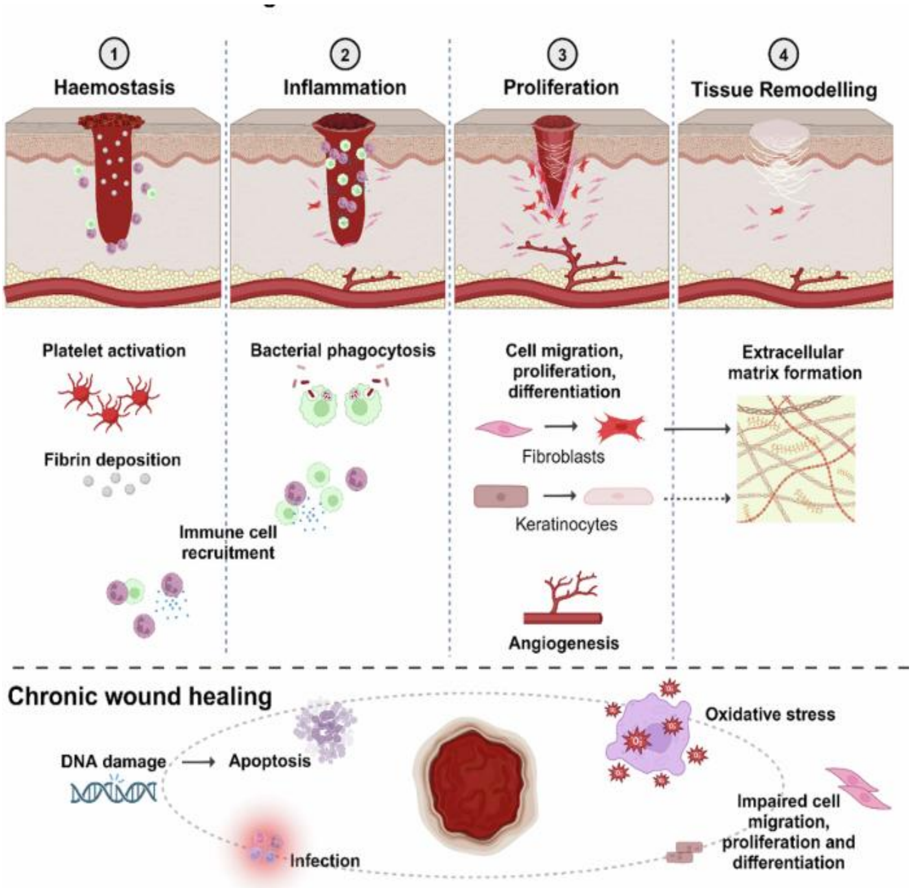


Figure 3: Molecular Pathways Involved in Saponin-Mediated Wound Healing Proposed schematic illustrating the regulatory effects of plant-based saponins on inflammatory mediators, antioxidant defense systems, growth factor signaling, collagen synthesis, and extracellular matrix remodeling during different phases of wound healing.

Source: Eming SA, Martin P, Tomic-Canic M. 2014. *Wound repair and regeneration: mechanisms, signaling, and translation.* **Science Translational Medicine**, 6(265):265sr6. https://doi.org/10.1126/scitranslmed.3009337

7. Advantages of Plant-Based Saponins Over Conventional Wound Healing Drugs

The rising research interest on the use of plant-based saponins in the care of wounds is highly informed by its comparative benefits over the traditional wound healing medications. Although synthetic therapies are usually narrowed to isolated targets, saponins possess a more comprehensive profile of therapy that is in keeping with wound healing becoming complex and multifactorial.

7.1 Multi-Target Mechanism of Action

https://doi.org/10.71058/jodac.v10i07003

The healing of wounds is a system of overlapping biological activities, which are inflammation regulation, oxidative stress regulation, angiogenesis, and extracellular matrix reorganization. The traditional wound healing medications normally act on one path, which can restrict the general efficiency. Plant-based saponins, on the contrary, provide their effects via a concomitant action on multiple molecular and cellular pathways. Saponins facilitate the coordinated wound healing in all stages of injury repair by regulating inflammatory mediators, enhancing antioxidant defenses, promoting collagen production via expression of growth factors, and sustaining wound healing in a coordinated manner. This multi target action promotes the success of therapeutic performance as well as decreasing treatment failure chances.

7.2 Reduced Adverse Effects

A variety of traditional wound healing preparations, especially antibiotics and synthetic anti-inflammatory treatment agents, are linked to such adverse effects as the delay of tissue healing and regeneration, cytotoxicity, and antimicrobial resistance. The available experimental research indicates that saponins found in plants have a good safety profile at the right dosage. They can induce a gradual response as opposed to being inhibitory and suppressive to the inflammatory responses, thus, leading to successful healing with fewer side effects. This property predisposes saponins to entrap them especially in cases of wound management and chronic wound care over the long run.

7.3 Cost-Effectiveness and Accessibility

Advanced wound care products and synthetic growth factor therapies are expensive and thus unable to be affordable formerly in low- and middle-income environments. Herbal plants that possess saponin are common and could be found in most areas sustainably. The relatively low price of extraction and formulation of plant-based saponins provides the economically feasible substitute to traditional treatments. This economic viability has big implications towards enhancing the accessibility of wound care in resource constrained healthcare systems.

7.4 Natural Origin and Better Biocompatibility

Plant-based saponins are naturally occurring and their biocompatibility with biological systems is attributed to high levels. This structural similarity to the endogenous compounds gives them an increase in their interaction with cell membranes and with cellular signaling pathways. Saponins have less probability of triggering severe immune or tissue irritation as compared to synthetic drugs in cases where properly formulated. Enhanced biocompatibility facilitates their use in topical preparations, dressing and multifaceted wound care preparations.

8. Limitations and Challenges

In spite of the future promising wound healing potential of plant-based saponins, there are a number of limitations and issues that need to be overcome before their large-scale use in clinical practice. These constraints need to be understood before future research can be conducted to enhance the translational value of experimental research.

8.1 Poor Bioavailability

https://doi.org/10.71058/jodac.v10i07003

A huge limitation relating to saponins is low bioavailability. Their complex chemical structure and high molecular weight make saponins less probable to be absorbed through biological membranes and less likely to be permeable too. When used as topicals, poor penetration by the drug through the skin could diminish treatment effects. Limitations may have unpredictable consequences on experimental studies and limit the effectiveness of such studies in clinical settings. Methods of increasing bioavailability are thus needed like upgraded delivery methods and formulating optimization.

8.2 Lack of Standardization of Plant Extracts

Saponin-rich plant extracts may have considerably different composition and the composition may change based on the plant species, provenance, circumstances at harvest and the method of extraction. This is a significant impediment to the replication of experimental data and comparison of results between studies due to this non-standardization. Differences in the content and purity of saponins would result in different therapeutic results. To possess reliability and reproducibility of the extraction protocols and quality control in saponin -based wound healing formulations, it is crucially necessary to have a standardized extraction protocol and quality control.

8.3 Dose Optimization Issues

The critical issue is to determine the best dose of saponins of plants. Although low to moderate dosage has indicated positive results in wound healing, high concentration could have cytotoxic or irritant effects. Most experimental trials vary dose schedules, the length of treatment, and the type of formulations and hence it becomes quite challenging to developmental and uniform dose instructions. Demanding dose -response studies are needed to obtain safe and effective therapeutic ranges.

8.4 Regulatory and Translational Challenges

Plant-based saponins are subject to serious regulatory obstacles to the transformation of their research findings to clinical implementation. Plant-based and herbal products may have no distinct development pathways as opposed to modern drugs. They have limited data on clinical trials, formulation variability, safety and efficacy concerns that make it slow to approve them. Further, to be able to bridge the gap between laboratory results and clinical practice, the challenges of translational studies on formulation stability, scaling and patient compliance should be designed to suit.

9. Future Perspectives

The emerging evidence on experimental findings shows the likelihood of plant-based saponins as wound healing critics. Nonetheless, further studies on these results demand a narrow and systematic effort to translate their findings into therapeutic options within some clinical setting. Advanced experimental design and translational approaches will play a significant role in assisting in bridging the current gaps to ensure that the incorporation of saponins into the modern wound care is successful.

https://doi.org/10.71058/jodac.v10i07003

9.1 Need for Well-Designed Clinical Trials

Although numerous in-vitro and in-vivo studies support the wound healing activity of saponins, clinical evidence remains limited. Well-designed randomized controlled trials are needed to evaluate their safety, efficacy, and therapeutic superiority over conventional treatments. Such studies should incorporate standardized formulations, appropriate dosing regimens, and clinically relevant endpoints. Generating robust clinical data will be essential to validate experimental findings and support regulatory approval.

9.2 Development of Nano-Formulations

The development of drug delivery systems has come up with bright options to address the bioavailability issues that are linked to saponins. Nano-formulations like nanoparticles, nanoemulsions and lipid-based carriers have the capacity to increase penetration across the skin and enhance stability as well as controlled release of active compounds. The addition of saponins to nano-based wound dressings or topical delivery systems could be of great impact in the therapeutic effect and compliance with the patient.

9.3 Target-Specific Molecular Investigations

Future research should focus on elucidating target-specific molecular mechanisms underlying saponin-mediated wound healing. Detailed investigation of signaling pathways involved in inflammation, angiogenesis, fibroblast activation, and extracellular matrix remodeling will provide deeper mechanistic insights. Such studies can aid in identifying molecular biomarkers of response and optimizing saponin-based therapies for specific wound types.

9.4 Scope for Translational and Clinical Research

The need to close the divide between the laboratory research and clinical practice is a priority. In order to guarantee applicability to the real world, translational studies that incorporate pharmacokinetics, formulation science as well as clinical wound assessment are required. Close researcher, clinician, and industry partner efforts can be used to develop high-quality, safe, and effective wound healing products based on saponins that can be used in clinical settings.

10. Conclusion

Wound healing is a complex biological process, which has to be organized to coordinate inflammation, oxidative stress, angiogenesis, and remodeling of the extracellular matrix. Regardless of the current developments in the standard wound treatment methodologies, the constraints in cost, safety, and the single-target method of treatment of the wound remains a problem to good wound management. Plant-based saponins have become promising bioactive molecules with immense wound healing ability in this case.

This is a systematic review of the experimental and molecular findings that pollute the contribution of saponins in wound healing. Results obtained in in-vivo and in-vitro experiments have shown that saponins promote the wound contraction process, enhance their epithelialization, enhance collagen synthesis and aids in angiogenesis. At a molecular scale, saponins balance major inflammatory mediators, reinforce antioxidant defense systems, control the expression of growth factors, and allocate controlled extracellular matrix

https://doi.org/10.71058/jodac.v10i07003

remodelling. The multi-mode actions make it possible to positively affect various steps of the wound healing process with the use of saponins.

Plant-based saponins have significant benefits over such conventional wound healing medication drugs, such as fewer adverse effects, higher biomatability and cost-effectiveness. Nevertheless, poor bioavailability, unstandardization of extracts, dose optimization, and regulatory obstacles are some of the issues that need to be overcome in order to have them used widely in clinical environments. New approaches e.g. the development of nano-formulations and target specific molecular studies have shown promise in eliminating these obstacles.

In general, saponins of plants can be considered as an excellent natural source of new wound healing therapeutics. Onward interdisciplinary research that includes experimental pharmacology, formulation science and clinical testing is necessary to get these compounds out of the bench to the bedside. Saponin-based therapy could have an important role in helping to improve modern wounds management with properly designed clinical trials and standardized methods.

References

1. Tartar, V. (1961). *The biology of Stentor*. Pergamon Press.
2. Gothard, E. J. (2016). *Wound healing, a multidisciplinary approach: Combining mathematical models and biological experiments* (Doctoral dissertation, University of Leeds, University of Sheffield, and University of York). White Rose eTheses Online. http://etheses.whiterose.ac.uk/17204/1/EGothardThesis_cor.pdf
3. Winciunas, P., & Lachman, D. (2021). Medical rehabilitation carried out by the Social Insurance Institution as part of disability to work prevention. *Acta Balneologica, 63*(3), 223–229. https://doi.org/10.36740/abal202103117
4. Sharma, A., Khanna, S., Kaur, G., & Singh, I. (2021). Medicinal plants and their components for wound healing applications. *Future Journal of Pharmaceutical Sciences, 7*(1), 1–13. https://doi.org/10.1186/s43094-021-00202-w
5. Vienna, C. F., Graz, R. B., Hohenheim, R. C., Milano, D. T., Trieste, A. T., & Wien, K. Z. (2007). Study on the assessment of plants/herbs, plant/herb extracts and their naturally or synthetically produced components as additives for use in animal production. *EFSA Supporting Publications, 4*(4). https://doi.org/10.2903/sp.efsa.2007.zn-001
6. Semwal, D. K. (2021). *Medicinal plants: Properties, uses and production*. Nova Science Publishers.
7. Gallo, P. (2012). *Bio-aesthetics and the artist as case history* (Doctoral dissertation, Concordia University). Spectrum Research Repository. https://spectrum.library.concordia.ca/975157/2/Gallo_PhD_S2013.pdf
8. Munodawafa, T. (2012). *Screening of some traditional medicinal plants from Zimbabwe for biological and antimicrobial activity* (Master's thesis). University of Zimbabwe. http://hdl.handle.net/10646/964
9. Kadhim, M. H., Jaafar, A. M., Abdoun, T. F., Abbas, H. L., & Mohammed, A. A. (2025). *Biomedical engineering: Principles, applications, and future trends*. Bright Sky Publications. https://doi.org/10.62906/bs.book.342
10. Abdelrahman, M., & Jogaiah, S. (2020). *Bioactive molecules in plant defense: Saponins*. Springer Nature.

https://doi.org/10.71058/jodac.v10i07003

11. Corriveau, D. M., & Fritsma, G. A. (1988). *Hemostasis and thrombosis in the clinical laboratory*. Lippincott Williams & Wilkins.
12. Ritchie, J. M., Rui, H., Zhou, X., Iida, T., Kodoma, T., Ito, S., Davis, B. M., Bronson, R. T., & Waldor, M. K. (2012). Inflammation and disintegration of intestinal villi in an experimental model for *Vibrio parahaemolyticus*-induced diarrhea. *PLoS Pathogens, 8*(3), e1002593. https://doi.org/10.1371/journal.ppat.1002593
13. Thakur, R., Jain, N., Pathak, R., & Sandhu, S. S. (2011). Practices in wound healing studies of plants. *Evidence-Based Complementary and Alternative Medicine, 2011*, 438056. https://doi.org/10.1155/2011/438056
14. Sharma, A., Khanna, S., Kaur, G., & Singh, I. (2021). Medicinal plants and their components for wound healing applications. *Future Journal of Pharmaceutical Sciences, 7*(1), Article 53. https://doi.org/10.1186/s43094-021-00202-w
15. Salehi, B., Azzini, E., Zucca, P., Varoni, E. M., Kumar, N. V. A., Dini, L., Panzarini, E., Rajkovic, J., Fokou, P. V. T., Peluso, I., Mishra, A. P., Nigam, M., El Rayess, Y., Beyrouthy, M. E., Setzer, W. N., Polito, L., Iriti, M., Sureda, A., Quetglas-Llabrés, M. M., & Sharifi-Rad, J. (2020). Plant-derived bioactives and oxidative stress-related disorders: A key trend towards healthy aging and longevity promotion. *Applied Sciences, 10*(3), 947. https://doi.org/10.3390/app10030947
16. Sharifi-Rad, J. (2020). Plant-derived bioactives and oxidative stress-related disorders: A key trend towards healthy aging and longevity promotion. *Applied Sciences, 10*(3), 947. https://doi.org/10.3390/app10030947
17. Hordyjewska, A., Ostapiuk, A., Horecka, A., & Kurzepa, J. (2019). Betulin and betulinic acid: Triterpenoid derivatives with a powerful biological potential. *Phytochemistry Reviews, 18*(3), 929–951. https://doi.org/10.1007/s11101-019-09623-1
18. Wang, B., Peng, M., Ma, D., Diao, Q., & Tu, Y. (2019). Saponin-induced shifts in the rumen microbiome and metabolome of young cattle. *Frontiers in Microbiology, 10*, 356. https://doi.org/10.3389/fmicb.2019.00356
19. Majumdar, A., & Sangole, P. (2016). Alternative approaches to wound healing. In *InTech eBooks*. https://doi.org/10.5772/63636
20. Majumder, P., & Paridhavi, M. (2019). A novel poly-herbal formulation hastens diabetic wound healing with potent antioxidant potential: A comprehensive pharmacological investigation. *Pharmacognosy Journal, 11*(2), 324–331. https://doi.org/10.5530/pj.2019.11.48
21. Ashfaq, U. A., Masoud, M. S., Nawaz, Z., & Riazuddin, S. (2011). Glycyrrhizin as an antiviral agent against hepatitis C virus. *Journal of Translational Medicine, 9*(1), 112. https://doi.org/10.1186/1479-5876-9-112
22. Muniandy, K., Gothai, S., Tan, W. S., Kumar, S. S., Esa, N. M., Chandramohan, G., Al-Numair, K. S., & Arulselvan, P. (2018). In vitro wound healing potential of stem extract of *Alternanthera sessilis*. *Evidence-Based Complementary and Alternative Medicine, 2018*, 3142073. https://doi.org/10.1155/2018/3142073
23. Herman, H. P. B. (2014). *Wound healing properties of Acrostichum aureum and Acrostichum speciosum on NIH/3T3 fibroblast cell lines and excisional wounds in rabbits*.
24. Alasbahi, R. H., & Groot, M. J. (2020). Evaluation of the wound healing activity of twelve herbal and non-herbal remedies used in Sana'a-Yemen for the treatment of wounds and burns. *Journal of Medicinal Herbs and Ethnomedicine, 6*, 90–116. https://doi.org/10.25081/jmhe.2020.v6.6379
25. Tebogo, M. O. (2004). *Separation and characterization of saponins from the bark extract of the South American soap bark tree (Quillaja saponaria Molina): Potential immuno-adjuvant active compounds*.

26. Kalluri, R., & Neilson, E. G. (2003). Epithelial-mesenchymal transition and its implications for fibrosis. *Journal of Clinical Investigation, 112*(12), 1776–1784. https://doi.org/10.1172/JCI200320530
27. Saithi, C., & Pashikanti, G. (2022). Wound healing potential of some medicinal plants. *International Journal of Pharmaceutical Sciences Review and Research, 77*(1), 106–116. https://doi.org/10.47583/IJPSRR.2022.V77I01.017
28. Nkadimeng, S. M., Steinmann, C. M., & Eloff, J. N. (2021). Anti-inflammatory effects of four psilocybin-containing magic mushroom water extracts in vitro on 15-lipoxygenase activity and on lipopolysaccharide-induced cyclooxygenase-2 and inflammatory cytokines in human U937 macrophage cells. *Journal of Inflammation Research, 14*, 3729–3738. https://doi.org/10.2147/JIR.S317182
29. Esposito, E., & Cuzzocrea, S. (2010). Antiinflammatory activity of melatonin in the central nervous system. *Current Neuropharmacology, 8*(3), 228–242. https://doi.org/10.2174/157015910792246155
30. Jain, S. K., Gupta, R., & Vengurlekar, S. (2025). *Applications of herbal excipients and polymers in wound healing*. IGI Global.
31. Bosch, F. X., Broker, T. R., Forman, D., Moscicki, A. B., Gillison, M. L., Doorbar, J., Stern, P. L., Stanley, M., Arbyn, M., Poljak, M., Cuzick, J., Castle, P. E., Schiller, J. T., Markowitz, L. E., Fisher, W. A., Canfell, K., Denny, L. A., Franco, E. L., Steben, M., ... de Sanjosé, S. (2013). Comprehensive control of human papillomavirus infections and related diseases. *Vaccine, 31*(Suppl. 7), G1–G31. https://doi.org/10.1016/j.vaccine.2013.10.002
32. Mani, R., Romanelli, M., & Shukla, V. (2012). *Measurements in wound healing: Science and practice*. Springer.
33. Khattak, S., Ullah, I., Sohail, M., Akbar, M. U., Rauf, M. A., Ullah, S., Shen, J., & Xu, H. (2024). Endogenous/exogenous stimuli-responsive smart hydrogels for diabetic wound healing. *Aggregate, 6*(2), e688. https://doi.org/10.1002/agt2.688
34. Babu, K., Subudhi, A., & Sabut, S. (2017). Segmentation of diabetic wound by multidimensional clustering for quantitative assessment of healing process. *Current Medical Imaging, 14*(1), 71–76. https://doi.org/10.2174/1573405613666161209104534
35. Ma, Z., Shou, K., Li, Z., Jian, C., Qi, B., & Yu, A. (2016). Negative pressure wound therapy promotes vessel destabilization and maturation at various stages of wound healing and thus influences wound prognosis. *Experimental and Therapeutic Medicine, 11*(4), 1307–1317. https://doi.org/10.3892/etm.2016.3083
36. Nadeem, H. R., Akhtar, S., Sestili, P., Ismail, T., Neugart, S., Qamar, M., & Esatbeyoglu, T. (2022). Toxicity, antioxidant activity, and phytochemicals of basil (*Ocimum basilicum* L.) leaves cultivated in Southern Punjab, Pakistan. *Foods, 11*(9), 1239. https://doi.org/10.3390/foods11091239
37. Waller, G. R., & Yamasaki, K. (2013). *Saponins used in traditional and modern medicine*. Springer Science & Business Media.
38. Duarte, J., Mascarenhas-Melo, F., Pires, P. C., Veiga, F., & Paiva-Santos, A. C. (2024). Multifunctional hydrogel-based therapies for chronic diabetic wound healing. *European Polymer Journal, 211*, 113026. https://doi.org/10.1016/j.eurpolymj.2024.113026
39. Lucas, T., Waisman, A., Ranjan, R., Roes, J., Krieg, T., Müller, W., Roers, A., & Eming, S. A. (2010). Differential roles of macrophages in diverse phases of skin repair. *The Journal of Immunology, 184*(7), 3964–3977. https://doi.org/10.4049/jimmunol.0903356

https://doi.org/10.71058/jodac.v10i07003

40. Miguel-Ruiz, J. E. S., & García-Arrarás, J. E. (2007). Common cellular events occur during wound healing and organ regeneration in the sea cucumber *Holothuria glaberrima*. *BMC Developmental Biology, 7*(1), 115. https://doi.org/10.1186/1471-213X-7-115
41. Bobbert, F. S. L., & Zadpoor, A. A. (2017). Effects of bone substitute architecture and surface properties on cell response, angiogenesis, and structure of new bone. *Journal of Materials Chemistry B, 5*(31), 6175–6192. https://doi.org/10.1039/C7TB00741H
42. Gardeazabal, L., & Izeta, A. (2024). Elastin and collagen fibres in cutaneous wound healing. *Experimental Dermatology, 33*(3), e15052. https://doi.org/10.1111/exd.15052
43. Winkler, J. (1999). *Apoptosis and inflammation*. Springer Science & Business Media.
44. Mann, C. J., Perdiguero, E., Kharraz, Y., Aguilar, S., Pessina, P., Serrano, A. L., & Muñoz-Cánoves, P. (2011). Aberrant repair and fibrosis development in skeletal muscle. *Skeletal Muscle, 1*(1), 21. https://doi.org/10.1186/2044-5040-1-21
45. Bala, K., & Sharma, Y. (2025). *Revolutionizing wound management: Formulating nanoparticles with tobacco stem bioactive compounds*. Cambridge Scholars Publishing.
46. Podolak, I., Grabowska, K., Sobolewska, D., Wróbel-Biedrawa, D., Makowska-Wąs, J., & Galanty, A. (2022). Saponins as cytotoxic agents: An update (2010–2021). Part II—Triterpene saponins. *Phytochemistry Reviews, 22*(1), 113–167. https://doi.org/10.1007/s11101-022-09830-3
47. Ivanov, D. A. (2015). *Ginsenosides, glycosidases and the ginseng–Pythium interaction*.
48. Oleszek, W., & Marston, A. (2013). *Saponins in food, feedstuffs and medicinal plants*. Springer Science & Business Media.
49. Adamson, B., Schwarz, D., Klugston, P., Gilmont, R., Perry, L., Fisher, J., Lindblad, W., & Rees, R. (1996). Delayed repair: The role of glutathione in a rat incisional wound model. *Journal of Surgical Research, 62*(2), 159–164. https://doi.org/10.1006/jsre.1996.0189

Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.