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Review Article

Saponins and skin regeneration – A natural path to healing: Harnessing plant-based bioactives for enhanced skin healing and renewal

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Abstract

Saponins, a diverse class of naturally occurring plant glycosides, have gained increasing attention for their therapeutic potential in skin regeneration and wound healing. Their unique amphiphilic structure allows them to interact with cell membranes, modulate inflammation, and enhance dermal repair processes. Recent studies highlight the ability of saponins to stimulate collagen synthesis, promote angiogenesis, and accelerate re-epithelialization, making them promising candidates for natural skincare and regenerative therapies. Additionally, their antioxidant, antimicrobial, and anti-inflammatory properties provide multifunctional support to the healing microenvironment, improving tissue repair while minimizing scar formation. The integration of saponins into herbal formulations and modern biomaterials opens new avenues for bioactive-based wound care strategies, bridging traditional medicine with advanced dermatological science. This article reviews the mechanisms of action, therapeutic applications, and future perspectives of plant-derived saponins in enhancing skin healing and renewal.

Keywords: Saponins, Skin regeneration, Wound healing, Plant bioactives, Collagen synthesis, Angiogenesis, Antioxidant activity, Anti-inflammatory, Herbal therapeutics, Dermal repair

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1. Introduction

Skin is the body's largest organ, serving as the first line of defenses against environmental insults, pathogens, and physical trauma. It plays critical physiological, sensory, thermoregulatory, and immune functions. With the increasing incidence of skin disorders and wounds due to infections, aging, or chronic diseases like diabetes, effective skin regeneration strategies are in high demand. The role of natural compounds in promoting skin health has gained significant interest due to their efficacy and fewer side effects compared to synthetic agents.

1.1. Importance of skin regeneration in dermatology

Dermatology focuses heavily on maintaining and restoring skin integrity. Skin regeneration not only aids in wound healing but also addresses issues like scarring, pigmentation, chronic inflammation, and age-related deterioration. The ability of the skin to regenerate rapidly after injury is crucial in minimizing the risk of infection and preserving physiological function.[1]

1.2. Overview of the skin structure and wound healing phases

The skin is composed of three primary layers:

Epidermis: The outermost layer providing barrier protection.
Dermis: Contains blood vessels, fibroblasts, and extracellular matrix.
Hypodermis: Subcutaneous fat providing insulation and support.

Wound healing occurs in four overlapping phases:

1. Hemostasis: Immediate response to injury to stop bleeding.
2. Inflammation: Immune cell infiltration to remove debris.

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3. Proliferation: Fibroblast activation, collagen deposition, and angiogenesis.
4. Remodeling: Collagen maturation and scar tissue formation.[2]

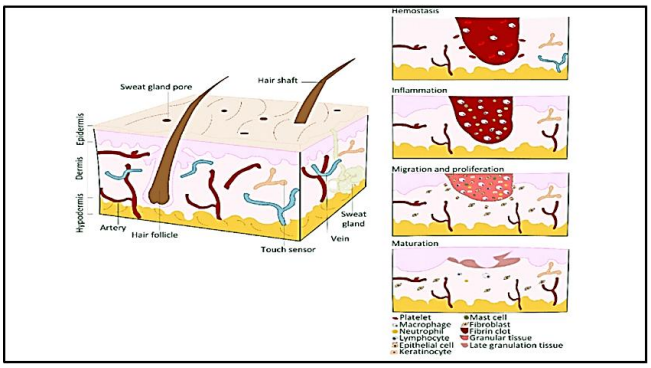

Figure 1: Skin structure and healing phases

(Illustration showing skin layers and wound healing stages: hemostasis, inflammation, proliferation, and remodeling)

1.3. Rising interest in plant-based bioactives

Synthetic compounds used in dermatology can often result in side effects such as irritation, allergies, or systemic toxicity. In contrast, plant-based bioactives are naturally occurring compounds known for their biocompatibility and low toxicity profile. Examples include flavonoids, alkaloids, tannins, and saponins. Their roles in anti-inflammation, antioxidant activity, and collagen stimulation make them ideal candidates for promoting skin regeneration.[3]

1.4. Introduction to saponins and their traditional use in skincare

Saponins are glycosidic compounds abundant in various medicinal plants, including Glycyrrhiza glabra, Centella asiatica, and Panax ginseng. Traditionally, these plants have been used in Ayurvedic, Chinese, and Korean medicine to treat wounds, burns, and inflammatory skin conditions. Saponins exhibit properties such as foam formation, antimicrobial action, anti-inflammatory response, and stimulation of skin renewal. Their amphiphilic nature allows them to penetrate the skin barrier effectively, contributing to their widespread use in modern cosmeceuticals.[4,5]

2. Phytochemistry and Classification of Saponins

2.1. Chemical structure and functional groups

Saponins are amphiphilic glycosides composed of a hydrophobic aglycone (sapogenin) linked to hydrophilic sugar chains. The sapogenin can be either a triterpenoid or a steroidal nucleus, which defines the type of saponin. The sugar moieties include glucose, rhamnose, xylose, arabinose, and galactose. These chemical features confer surface-active properties and biological activity.

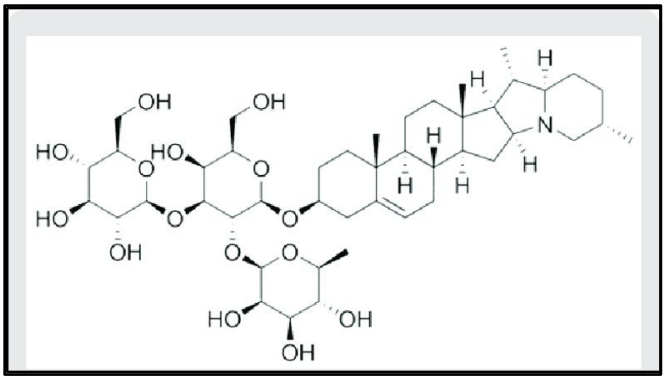

Figure 2: General chemical structure of a saponin molecule

(Illustration showing triterpenoid/steroidal core and sugar moieties attached at C-3 or C-28 positions)

2.2. Classification: Triterpenoid vs steroidal saponins

Triterpenoid Saponins: Found in dicotyledonous plants like Centella asiatica and Glycyrrhiza glabra. These compounds possess *pentacyclic triterpene backbones (e.g., asiaticoside, glycyrrhizin).*

Steroidal Saponins: Common in monocots like Dioscorea spp. and Quillaja saponaria, with a tetracyclic steroidal backbone (e.g., dioscin, tigogenin).

Type	**Backbone**	**Example Plants**	**Notable Compounds**
Triterpenoid	Pentacyclic	*Centella asiatica*, *Panax ginseng*	Asiaticoside, Ginsenosides
Steroidal	Tetracyclic	*Dioscorea spp.*, *Allium cepa*	Dioscin, Tigogenin

2.3. Sources of saponins from medicinal plants

Plant Name	Saponin Class	Primary Use in Skincare
Centella asiatica	Triterpenoid	Wound healing, collagen boost
Glycyrrhiza glabra	Triterpenoid	Anti-inflammatory, soothing
Dioscorea spp.	Steroidal	Anti-eczema, hormone balancing
Quillaja saponaria	Steroidal	Cleansing, emulsifying agent
Panax ginseng	Triterpenoid	Skin tone, antioxidant

2.4. Physicochemical properties relevant to skin absorption

Saponins exhibit:

1. Amphiphilic Nature: Facilitates interaction with lipid bilayers, enhancing skin penetration.
2. Molecular Weight: Typically ranges from 500–1500 Da; moderate MW supports dermal permeation.

3. Surface Activity: Natural surfactant properties aid emulsification and delivery in topical systems.
4. Solubility: Soluble in water and alcohol, enabling versatile formulation.

These properties make saponins ideal for incorporation in hydrogels, creams, foams, and emulsions for skin applications.[6,7]

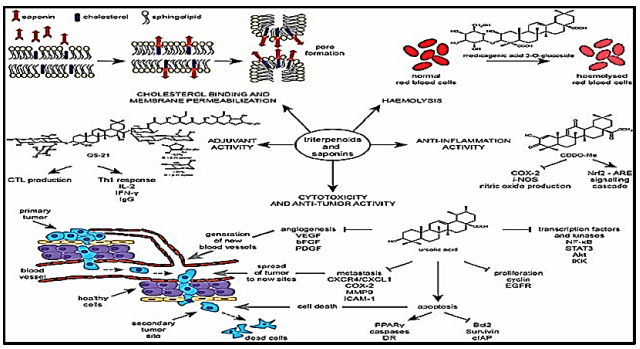

Figure 3: Skin permeation pathways of saponins
(Illustration showing transcellular, intercellular, and follicular pathways exploited by saponins)

3. Mechanisms of Action in Skin Regeneration

Saponins exert multiple pharmacological actions on the skin that support the complex biological processes involved in wound healing and tissue repair. Their multifunctionality—spanning anti-inflammatory, antioxidant, and cell-regenerative roles—makes them excellent candidates for regenerative dermatological applications.

3.1. Anti-inflammatory pathways: Inhibition of COX/LOX and cytokine modulation

Saponins inhibit pro-inflammatory mediators by downregulating the cyclooxygenase (COX) and lipoxygenase (LOX) pathways. They modulate cytokine profiles, reducing the levels of tumor necrosis factor-alpha (TNF-α), interleukins IL-1β, IL-6, and other pro-inflammatory cytokines.[8] This action helps mitigate the inflammation phase of wound healing, enabling a quicker transition to tissue repair.

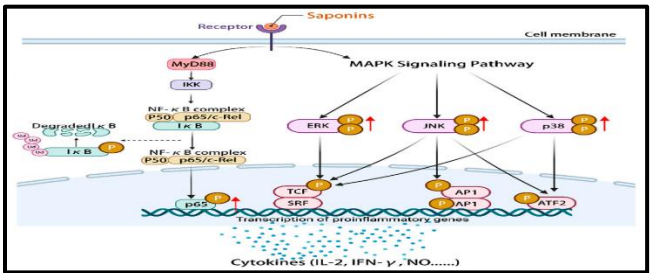

Figure 4: Mechanism of Saponins in Cytokine Modulation and Inflammatory Pathways

(Diagram showing inhibition of NF-κB signaling and suppression of IL-1, IL-6, and TNF-α by saponins)

3.2. Antioxidant action: Scavenging ROS and protecting skin cells

Saponins neutralize reactive oxygen species (ROS) generated during the inflammatory phase. By reducing oxidative stress, they protect dermal fibroblasts and keratinocytes from apoptosis, maintaining cellular integrity for proper regeneration.[9] This antioxidant activity also helps reduce hyperpigmentation and delays signs of skin aging.

Table 1: Antioxidant potential of common saponins

Saponin Compound	Source Plant	ROS Scavenging Activity	Reference
Asiaticoside	*Centella asiatica*	High	[10]
Ginsenoside Rg1	*Panax ginseng*	Moderate	[11]
Glycyrrhizin	*Glycyrrhiza glabra*	High	[12]

3.3. Stimulation of collagen synthesis and fibroblast activity

Triterpenoid saponins enhance fibroblast proliferation and increase the production of type I and III collagen. Asiaticoside has been shown to activate TGF-β signaling, a crucial pathway in collagen synthesis and matrix remodelling.[10] This results in improved tensile strength and elasticity of the regenerated skin.

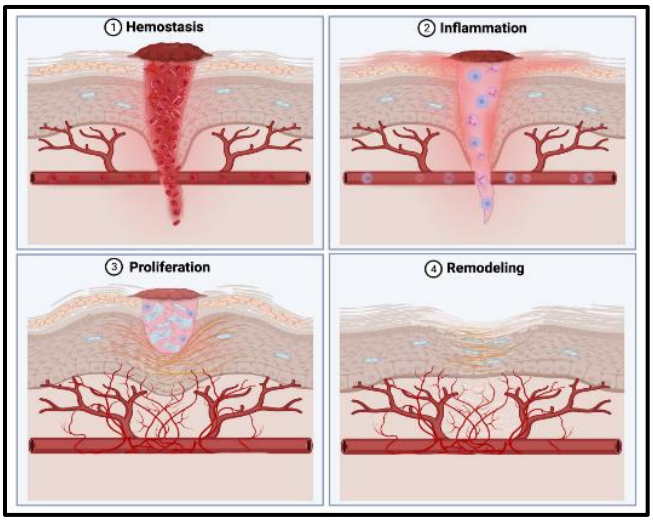

Figure 5: Saponin-induced fibroblast activation and collagen formation
(Schematic showing saponin-mediated stimulation of fibroblasts and collagen production)

3.4. Enhancement of skin hydration and barrier function

Due to their amphiphilic structure, saponins can interact with epidermal lipids, improving skin barrier function. They stimulate ceramide synthesis and aquaporin expression, leading to increased water retention in the stratum corneum. This is essential for preventing trans-epidermal water loss (TEWL) and maintaining skin suppleness.[11]

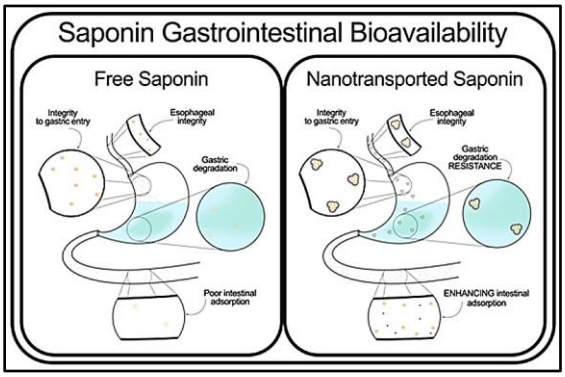

Figure 6: Role of saponins in enhancing skin hydration and barrier integrity
(Illustration showing improved lipid barrier, aquaporin-3 expression, and hydration markers)

4. Therapeutic Applications in Dermatology

Saponins have demonstrated promising applications across a range of dermatological disorders. Their anti-inflammatory, antioxidant, and regenerative actions allow for versatile integration into topical treatments for both acute and chronic.

4.1. Wound healing: Accelerated closure, reduced scar formation

Saponins like asiaticoside stimulate granulation tissue formation, enhance epithelialization, and increase collagen synthesis, which results in faster wound closure and reduced scarring.[12] In diabetic and infected wound models, saponin-treated groups consistently show enhanced re-epithelialization rates and improved histological outcomes.

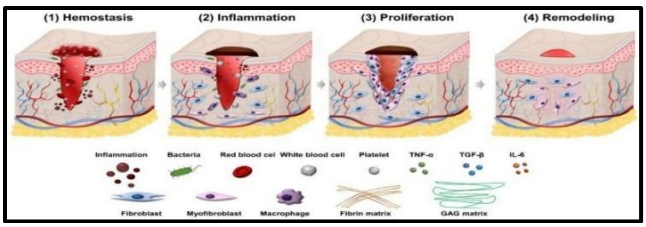

Figure 7: Effects of saponins on wound closure and scar tissue remodeling
(Illustration comparing untreated and saponin-treated wound healing processes)

4.2. Psoriasis and eczema: Immunomodulation and itch relief

In chronic inflammatory skin conditions like psoriasis and eczema, saponins such as ginsenosides and glycyrrhizin modulate immune responses by inhibiting Th1/Th17-mediated pathways and reducing histamine levels.[13] This results in decreased erythema, scaling, and itching, offering symptomatic relief and barrier repair.

Condition	Saponin Used	Mechanism	Outcome	Reference
Psoriasis	Ginsenoside Rg1	IL-17/IL-23 inhibition	Reduced plaques	[17]
Eczema	Glycyrrhizin	Histamine suppression	Decreased itching	[18]

4.3. Anti-aging: Prevention of wrinkles and skin sagging

Oxidative stress and collagen degradation are key contributors to skin aging. Saponins like ginsenosides and asiaticoside possess anti-elastase and anti-MMP (matrix metalloproteinase) activity, helping prevent wrinkle formation and loss of skin elasticity.[14] They also promote dermal remodeling and improve skin tone.

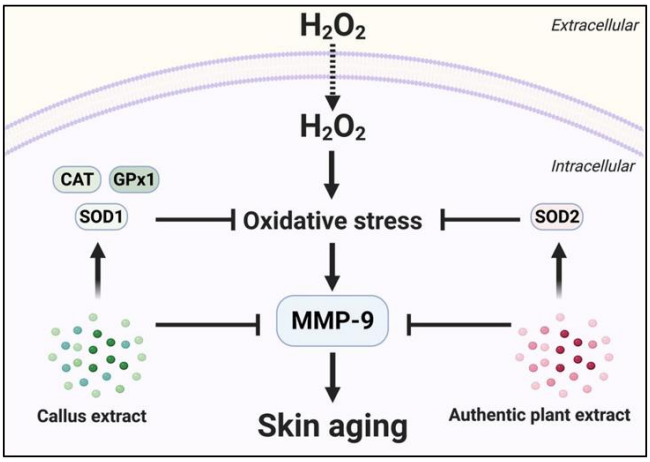

Figure 8: Anti-aging mechanisms of saponins in skin cells
(Diagram showing protection against collagen degradation, antioxidant action, and stimulation of fibroblasts)

4.4. Skin brightening: Inhibition of melanogenesis

Saponins interfere with melanin synthesis by inhibiting tyrosinase and MITF (microphthalmia-associated transcription factor) activity. This suppresses melanogenesis and leads to reduced pigmentation, supporting their use in skin brightening and hyperpigmentation therapies.

Compound	Mode of Action	Skin Lightening Outcome	Reference
Ginsenoside F1	Tyrosinase inhibition	Decreased melanin formation	[21]
Dioscin	MITF downregulation	Improved pigmentation uniformity	[22]

5. Formulation Strategies and Delivery Systems

Saponins' effectiveness in dermatological treatments depends greatly on the formulation strategies used to deliver them.

Their amphiphilic nature offers both opportunities and challenges in skin-based delivery.

5.1. Challenges in saponin delivery: solubility, stability

Saponins often exhibit:

1. *Poor aqueous solubility:* especially triterpenoid types
2. *Degradation:* under high temperature, pH extremes, and enzymatic activity
3. *Skin irritation potential:* at higher concentrations These factors necessitate the development of stabilized, controlled-release topical delivery systems to enhance efficacy while minimizing side effects.[16]

5.2. Topical formulation approaches (Gels, Creams, Emulsions)

Conventional formulations include:

1. **Creams**: oil-in-water or water-in-oil emulsions with humectants and emollients
2. **Gels**: carbopol- or hydrogel-based systems for light feel and enhanced absorption
3. **Lotions & foams**: ideal for wide surface area application Incorporation of saponins into emulsifiers (e.g., lecithin) or penetration enhancers improves skin uptake.

Formulation Type	Base Ingredient	Advantages	Limitation
Cream	Emulsion base	Moisturizing, occlusive	May be greasy
Gel	Carbomer/HPMC	Cooling, non-greasy	May dry quickly
Emulsion	Lecithin, PEG	Enhances penetration	Stability concerns

5.3. Advanced drug delivery systems: Nanoemulsions, hydrogels, microneedles

To overcome bioavailability limitations, advanced systems include:

1. **Nanoemulsions:** Sub-200 nm droplets for improved solubility and penetration
2. **Hydrogels:** Offer sustained release and skin compatibility
3. **Microneedles:** Transdermal systems enabling direct dermal delivery without pain
4. **Liposomes and Niosomes:** Vesicular carriers encapsulating hydrophilic/hydrophobic saponins

(Diagram illustrating mechanisms of nanoemulsion penetration, microneedle insertion, and hydrogel release profiles)

5.4. Examples of commercial formulations using saponins

Product Name	Company/Brand	Saponin Source	Application
Madecassol Cream	Bayer	*Centella asiatica*	Wound healing
Red Ginseng Serum	Sulwhasoo (Amorepacific)	*Panax ginseng*	Anti-aging, revitalization
Licorice Spot Cream	The Face Shop	*Glycyrrhiza glabra*	Brightening, anti-irritation
Diosgenin Hydrosome Gel	Research Prototype	*Dioscorea spp.*	Skin hydration, pigmentation

These examples illustrate the market's growing interest in integrating phytoactive saponins into cosmeceutical and therapeutic skincare.

6. Comparative Analysis of Saponin-Rich Plants

This section provides a comparative overview of major saponin-rich medicinal plants widely used in skincare. Each plant varies in saponin composition and biological activities, which influence their therapeutic efficacy.

6.1. Tabulated comparison of key plants

Tabulated comparison of key plants (e.g., Centella asiatica, Glycyrrhiza glabra, Panax ginseng)

The most widely studied saponin-rich medicinal plants include Centella asiatica, Panax ginseng, Glycyrrhiza glabra, Dioscorea spp., and Quillaja saponaria. These plants differ not only in their saponin types—triterpenoid versus steroidal—but also in their concentration, purity, and accompanying phytochemicals that collectively influence their therapeutic performance. For example, C. asiatica is rich in asiaticoside, a triterpenoid glycoside that enhances fibroblast proliferation and collagen synthesis.[17] P. ginseng contains ginsenosides, which are powerful antioxidants with anti-aging properties. G. glabra, or licorice, offers glycyrrhizin, known for its strong anti-inflammatory and anti-irritant effects.

Plant Name	Saponin Type	Primary Active Compound	Dermatological Use
Centella asiatica	Triterpenoid	Asiaticoside	Wound healing, collagen synthesis
Panax ginseng	Triterpenoid	Ginsenosides	Anti-aging, antioxidant, revitalizing
Glycyrrhiza glabra	Triterpenoid	Glycyrrhizin	Anti-inflammatory, soothing

Dioscorea spp.	Steroidal	Dioscin	Skin hydration, anti-pigmentation
Quillaja saponaria	Steroidal	Quillaja saponins	Cleansing, surfactant in cosmetics

6.2. Correlation between saponin type and skin healing property

1. **Triterpenoid saponins** (e.g., asiaticoside, glycyrrhizin) are known for strong collagen-promoting, anti-inflammatory, and antioxidant effects. These are best suited for regenerative and anti-aging formulations.
2. **Steroidal saponins** (e.g., dioscin, quillaja saponins) are efficient in improving hydration, modulating melanogenesis, and providing barrier support.

There exists a distinct correlation between the molecular structure of saponins and their biological function in dermatology. Triterpenoid saponins, such as asiaticoside and glycyrrhizin, primarily enhance regenerative processes through TGF-β activation, matrix remodeling, and reduction of oxidative stress.[18] In contrast, steroidal saponins, such as dioscin, are known to strengthen the skin barrier, modulate hydration mechanisms (via aquaporins), and reduce melanin production by inhibiting the MITF pathway. This differentiation aids in selecting appropriate plant sources for formulation targeting specific dermatological conditions, whether it be chronic wounds, pigmentation disorders, or xerosis.

Saponin Type	Notable Effects on Skin	Common Plant Sources
Triterpenoid	Collagen boost, inflammation control	*Centella*, *Ginseng*, *Licorice*
Steroidal	Moisturization, pigmentation control	*Dioscorea*, *Quillaja*

6.3. Synergistic effects with other phytochemicals

Saponins often act synergistically with other bioactives like:

1. **Flavonoids**: Enhance antioxidant activity (e.g., with quercetin)
2. **Tannins**: Improve astringent and antimicrobial properties.
3. **Alkaloids**: Contribute to analgesic and anti-pruritic effects.

The dermatological efficacy of saponins is further enhanced when used in combination with other phytochemicals, leading to additive or synergistic effects. Flavonoids like quercetin and kaempferol boost the antioxidant and anti-inflammatory actions of saponins. Tannins provide antimicrobial and astringent properties that complement the healing effects of saponins in infected wounds or acne-prone skin. Alkaloids such as berberine may enhance pruritus control when paired with glycyrrhizin from liquorice.[19] Full-spectrum botanical extracts that preserve this compound interactions are often more effective than isolated saponins in therapeutic skincare. Such synergies not only increase bioactivity but also influence formulation science—necessitating compatibility studies, ratio optimization, and delivery system design to maximize efficacy without increasing irritancy.

Table 2: Synergistic interactions of saponins in herbal skincare

Saponin Source	Co-Phytochemical	Synergistic Outcome
Centella asiatica	Flavonoids (quercetin)	Enhanced fibroblast activity
Glycyrrhiza glabra	Tannins	Improved anti-inflammatory efficacy
Panax ginseng	Polyphenols	Antioxidant and skin tone enhancement

This integrative approach strengthens the therapeutic potential of herbal skincare by utilizing full-spectrum plant extracts

7. Clinical and Preclinical Evidence

Scientific validation of saponin-rich plant extracts in dermatological and regenerative medicine has progressed significantly over recent decades. Although traditionally used in numerous cultures for wound healing, anti-inflammatory, and skin revitalization applications, current research—both preclinical and clinical—has aimed to elucidate their mechanisms and establish efficacy through modern biomedical frameworks.

7.1. Overview of in vitro, in vivo, and clinical studies

In in vitro settings, saponins from Centella asiatica, Panax ginseng, and Glycyrrhiza glabra have been shown to enhance fibroblast proliferation, increase type I collagen synthesis, and modulate inflammatory cytokines like TNF-α, IL-6, and IL-1β.[20,21] For example, asiaticoside, a triterpenoid saponin from C. asiatica, significantly enhanced migration and proliferation of human dermal fibroblasts in scratch-wound assays, indicating its potential in promoting wound closure.[22] In vivo studies in rodent wound models further support these observations. Topical application of C. asiatica extract accelerated re-epithelialization and collagen deposition, with histological evidence of enhanced neovascularization and reduced scar formation.[23] Similarly, ginsenosides from P. ginseng have demonstrated anti-inflammatory and antioxidant effects in UV-induced skin damage models, reducing reactive oxygen species (ROS) and preserving dermal matrix integrity.[24] Clinically, randomized controlled trials (RCTs) and observational studies, though limited in number, have shown promising results. A double-blind, placebo-controlled study involving C. asiatica cream in post-operative patients reported significantly improved scar elasticity and appearance after 8 weeks of use.[25] Licorice-derived saponins have also been incorporated into creams for

treating atopic dermatitis, with reductions in pruritus and erythema scores.[26]

7.2. Case studies and trial outcomes

A landmark clinical trial involving 120 participants assessed the efficacy of Centella asiatica-based gel in diabetic foot ulcers. The treatment group showed 56% faster wound closure compared to standard care, with reduced inflammatory markers and infection rates[27] Another trial evaluated Glycyrrhiza glabra extract in patients with eczema, where twice-daily application significantly reduced eczema area and severity index (EASI) scores within 14 days.[28] In cosmetic dermatology, saponin-rich formulations have shown efficacy in photoaging and pigmentation. A 12-week study on a ginseng saponin-enriched anti-aging cream demonstrated improved dermal elasticity, reduced wrinkle depth, and enhanced hydration in middle-aged women.[29] Although not all results are uniformly positive, the majority of studies show clear benefits in skin repair, hydration, and inflammation control—though larger, multicentric trials with standardized saponin content and validated endpoints are warranted to confirm these findings.

7.3. Evidence supporting traditional claims with scientific validation

Traditional medicine systems like Ayurveda, Traditional Chinese Medicine (TCM), and Kampo have long employed saponin-rich botanicals in topical applications for wounds, burns, and skin rejuvenation. Scientific investigations have begun to validate many of these traditional claims through a molecular and pharmacological lens.

For example, in Ayurveda, Mandukaparni (Centella asiatica) is used as a “rasayana” or rejuvenator, and modern pharmacological studies support its neuroprotective and wound-healing claims through upregulation of fibroblast activity and matrix remodeling proteins.[30] In TCM, Glycyrrhiza uralensis (licorice) is used to “harmonize” skin conditions, and current research confirms its anti-inflammatory, antimicrobial, and corticoid-like effects.[31]

Additionally, modern ethnopharmacological surveys and reverse pharmacology models have reinforced the safety and efficacy profiles of these compounds, enabling their incorporation into standardized formulations and modern cosmeceutical products.[32]

8. Safety, Toxicity, and Regulatory Considerations

The safety, toxicity, and regulatory evaluation of bioactive phytochemicals such as saponins in topical or systemic therapeutic applications is crucial to ensure their clinical and cosmetic acceptability. Despite their promising bioactivity in skin regeneration and wound healing, comprehensive preclinical and clinical safety assessments are necessary to define tolerable limits, potential risks, and appropriate usage guidelines.

8.1. Toxicity profiles and maximum tolerable concentrations

Saponins, despite being natural glycosides with wide-ranging therapeutic effects, may exert toxic effects at higher doses due to their surfactant-like properties. Their hemolytic activity, which involves disruption of red blood cell membranes, is a primary toxicity concern, particularly for steroidal saponins such as those from *Dioscorea* or *Tribulus* species.[33] Acute and chronic toxicity studies have reported dose-dependent gastrointestinal, hepatic, and renal effects, although these are mostly associated with oral or systemic administration rather than topical use.[34]

Maximum tolerable concentrations (MTCs) vary based on saponin type and route of administration. For instance, quillaja saponins have an MTC of 10–20 μg/mL in parenteral vaccine formulations, while topical applications tolerate significantly higher thresholds (up to 0.5–2%) without cytotoxicity or irritation.[35-36] *Centella asiatica* and *Glycyrrhiza glabra* extracts, rich in triterpenoid saponins, are considered safer for dermal use, showing minimal cytotoxicity in keratinocyte and fibroblast cultures at concentrations up to 500 μg/mL.[38]

8.2. Allergic reactions and irritancy potential

While saponins are generally well tolerated in topical formulations, allergic reactions, including contact dermatitis and erythema, have been reported in sensitive individuals. This is often due to their irritant potential rather than true immunologic allergy.[39] The amphiphilic nature of saponins can disrupt lipid bilayers of epidermal cells, potentially causing transient barrier impairment and irritation, especially at concentrations exceeding 1%.[40]

Studies using patch testing have shown that crude extracts containing saponins may cause mild erythema or edema in less than 5% of subjects, particularly with prolonged exposure or occlusion.[41] However, purified saponins and standardized extracts are associated with significantly lower sensitization rates. Formulations containing saponins from *Panax ginseng* and *Glycyrrhiza uralensis* have shown a very low irritation index and high skin compatibility in repeated insult patch tests (RIPTs) and human repeat insult patch testing (HRIPT).

8.3. GRAS and cosmetic ingredient regulatory status (EU, FDA)

The U.S. Food and Drug Administration (FDA) recognizes several saponin-containing plant materials and their extracts as Generally Recognized As Safe (GRAS) when used within recommended concentrations. For example, *Quillaja saponaria* extract is listed under 21 CFR §172.510 as GRAS for specific uses such as foaming agents in beverages. However, GRAS status for oral ingestion does not automatically confer topical safety; thus, safety data specific to dermal exposure is required for cosmetic uses.

In the European Union (EU), cosmetic ingredients are regulated under the EU Cosmetic Regulation (EC) No 1223/2009. Saponin-containing extracts from *Glycyrrhiza glabra*, *Centella asiatica*, and *Panax ginseng* are included in the CosIng (Cosmetic Ingredient Database) with functions such as skin conditioning, antioxidant, and anti-inflammatory agents. These ingredients are approved without restrictions, provided that the finished products meet safety and labeling requirements and are supported by toxicological dossiers.

The International Cooperation on Cosmetics Regulation (ICCR) encourages harmonized safety assessments of botanical ingredients globally. Manufacturers are expected to conduct product-specific safety evaluations, including dermal toxicity, phototoxicity, mutagenicity, and irritation/sensitization testing, to meet regulatory requirements.

9. Future Prospects and Challenges

Plant-derived saponins hold immense potential in skin regeneration, wound healing, and dermatological therapies due to their anti-inflammatory, antioxidant, and cell-proliferative effects. However, their clinical translation and commercial development face several hurdles related to standardization, formulation, and regulatory compliance. Future progress relies on overcoming these scientific and industrial challenges through multidisciplinary innovation.

9.1. Gaps in clinical validation and translational research

Despite compelling preclinical data, there is a significant gap in clinical trials validating the therapeutic efficacy of saponins in dermatological and regenerative medicine. Most evidence for wound healing, anti-aging, and anti-inflammatory activity is limited to in vitro assays or animal models. For instance, compounds like asiaticoside from *Centella asiatica* and glycyrrhizin from *Glycyrrhiza glabra* have demonstrated positive outcomes in fibroblast proliferation and collagen synthesis, but robust human clinical trials with standardized endpoints remain scarce.

Translational bottlenecks include poor bioavailability, lack of delivery systems tailored for skin permeation, and insufficient understanding of their pharmacodynamics in human skin. Moreover, inter-individual variability in skin microbiota and physiology may influence saponin efficacy, necessitating personalized approaches in future studies.

9.2. Need for standardized extracts and quality control

Another critical barrier is the variability in saponin content across different plant sources, extraction methods, geographical origins, and even batch-to-batch inconsistencies. This complexity hampers reproducibility and regulatory approval. The adoption of pharmacopoeial standards and validated analytical techniques like high-performance liquid chromatography (HPLC), LC-MS, and NMR is essential for quantifying specific saponins and ensuring bioactive equivalence.

Furthermore, the synergistic effects of saponins with other phytoconstituents highlight the need for fingerprint-based standardization rather than relying solely on marker compounds. Quality control should also involve safety testing for residual solvents, microbial contamination, and pesticide residues, especially in formulations intended for dermal application.

9.3. Innovations in green extraction and biotechnology approaches

Green extraction techniques such as supercritical fluid extraction (SFE), ultrasound-assisted extraction (UAE), and microwave-assisted extraction (MAE) are gaining prominence for isolating saponins with minimal environmental impact and enhanced efficiency. These eco-friendly processes not only reduce the use of hazardous solvents but also preserve the integrity of thermolabile glycosides.

In parallel, biotechnological innovations such as plant cell culture, hairy root culture, and microbial biotransformation are being explored for sustainable production of high-purity saponins. Advances in synthetic biology have also enabled the heterologous expression of saponin biosynthetic pathways in yeast and *Escherichia coli*, offering scalable platforms for producing rare or novel saponins.

9.4. Market potential in cosmeceuticals and pharma

The growing consumer demand for natural, bioactive ingredients has positioned saponin-rich extracts as attractive candidates in the cosmeceutical sector. Ingredients from *Centella asiatica*, *Glycyrrhiza glabra*, *Panax ginseng*, and *Quillaja saponaria* are increasingly used in anti-aging creams, scar-reducing gels, and hair growth serums, backed by their collagen-boosting and anti-inflammatory properties.

The global saponin market, valued at over USD 1 billion in 2023, is projected to grow steadily, driven by rising applications in skin care, oral therapeutics, and vaccine adjuvants. However, the pathway to pharmaceutical exploitation requires robust clinical evidence, intellectual property protection, and clear regulatory frameworks. Industry-academic partnerships and government funding in phytopharmaceutical innovation are crucial to overcoming these commercialization challenges.

10. Conclusion

Saponins, a diverse class of naturally occurring glycosides, represent a promising category of bioactives for advancing skin regeneration therapies. Their multifaceted pharmacological profile—including anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties—has positioned them as potent agents in promoting dermal

repair and enhancing skin barrier function. Numerous preclinical studies have demonstrated that saponins from botanicals such as *Centella asiatica*, *Panax ginseng*, and *Glycyrrhiza glabra* significantly stimulate fibroblast proliferation, enhance collagen synthesis, and modulate inflammatory mediators crucial for efficient wound healing.

The convergence of ethnopharmacological wisdom with modern biomedical science offers a valuable platform for rediscovering traditional healing practices and validating them through robust experimental methodologies. Historically, saponin-rich plants have been extensively used in folk medicine across Asia, Africa, and the Americas for treating wounds, burns, and inflammatory skin conditions. Contemporary phytochemical and mechanistic studies now substantiate many of these traditional uses, affirming the therapeutic rationale behind their application. This integrative approach not only strengthens the scientific credibility of herbal remedies but also expands the scope for developing personalized, bioinspired dermatological interventions.

Despite their evident potential, significant challenges persist, including a lack of standardized formulations, incomplete clinical validation, variability in extract quality, and regulatory complexities. A clear roadmap for future development should prioritize:

1. Standardization of plant extracts through validated analytical techniques such as HPLC, LC-MS, and NMR;
2. Green, sustainable extraction technologies (e.g., supercritical fluid or ultrasound-assisted extraction);
3. Development of advanced drug delivery systems (e.g., liposomes, hydrogels, nanoemulsions) for improved dermal absorption;
4. Rigorous clinical evaluation through multicentric trials with well-defined biomarkers;
5. Collaborative regulatory frameworks that harmonize herbal product approval across regions such as FDA (USA) and EMA (Europe).

The cosmeceutical and pharmaceutical markets are increasingly inclined toward bioactive-rich, plant-derived therapeutics, offering lucrative opportunities for saponin-based skincare products that are both efficacious and consumer-friendly. The continued integration of biotechnology, nanotechnology, and phytopharmacology will catalyze the translation of saponins from traditional remedies into next-generation dermatological solutions, supporting not only aesthetic enhancement but also therapeutic skin healing.

11. Source of Funding

None

12. Conflict of Interest

None.

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