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Role of Sea Buckthorn in Skin Regeneration and Wound Healing: Mechanisms and Clinical Evidence

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ABSTRACT

Sea buckthorn (*Hippophae rhamnoides*), a deciduous shrub from the family Elaeagnaceae, has gained increasing attention due to its rich composition of bioactive compounds including flavonoids, carotenoids, polyunsaturated fatty acids, vitamins (especially C and E), and phytosterols. These constituents have shown promising results in dermatological and regenerative medicine. Sea buckthorn oil, derived from its berries and seeds, has demonstrated efficacy in promoting skin regeneration, reducing inflammation, enhancing epithelialization, and accelerating wound healing. This paper provides a comprehensive review of the molecular mechanisms through which sea buckthorn exerts its effects on skin repair, including its antioxidant activity, modulation of cytokine expression, stimulation of collagen synthesis, and promotion of angiogenesis. Furthermore, the review highlights preclinical studies and clinical trials that support its therapeutic potential in managing burns, surgical wounds, ulcers, and dermatological conditions like eczema and atopic dermatitis. The safety profile and formulation strategies for topical and oral use are also discussed, making a case for the integration of sea buckthorn in evidence-based wound care regimens.

1. Introduction

Wound healing is a vital biological process that ensures the restoration of skin integrity after injury. The skin, being the largest and most exposed organ of the body, frequently undergoes trauma due to mechanical injuries, burns, surgeries, and various dermatological conditions. The process of healing involves a highly regulated cascade of cellular and molecular events, encompassing hemostasis, inflammation, proliferation, and remodelling phases. Any disruption or delay in these processes can result in chronic wounds, infections, hypertrophic scarring, or incomplete tissue repair. Consequently, the development of effective, safe, and affordable therapeutic agents to enhance wound healing has become a major focus in both biomedical and pharmaceutical research.

Among various natural remedies being explored, *Hippophae rhamnoides*, commonly known as sea buckthorn, has emerged as a promising candidate for skin regeneration and wound care. Native to Europe and Asia, sea buckthorn is a deciduous shrub of the family Elaeagnaceae and is well-known in traditional Tibetan, Mongolian, and Ayurvedic medicine. The plant is valued for its berries, leaves, and seeds, which are rich in a wide array of bioactive compounds including vitamins (notably vitamins C and E), polyunsaturated fatty acids (omega-3, -6, -7, and -9), carotenoids, flavonoids, sterols, and amino acids. These constituents exhibit potent antioxidant, anti-inflammatory, antimicrobial, and tissue-regenerating properties that collectively contribute to the healing process.

In particular, sea buckthorn oil derived from the fruit pulp and seeds has shown significant efficacy in accelerating cutaneous wound repair. Its use in topical preparations such as creams, ointments, and hydrogel dressings has been associated with improved wound contraction, epithelialization, angiogenesis, and collagen deposition in various experimental models. The oil's rich content of palmitoleic acid (omega-7), which is also a natural component of human skin sebum, plays a crucial role in maintaining skin elasticity, hydration, and barrier function. Additionally, flavonoids like quercetin and kaempferol in sea buckthorn exhibit anti-inflammatory actions by modulating cytokine levels, while carotenoids contribute to epithelial repair and photoprotection.

With the increasing global interest in plant-based dermatological agents, sea buckthorn has garnered attention not only for its pharmacological effects but also for its safety profile and adaptability in formulation science. Several in vitro studies have confirmed its role in promoting the proliferation and migration of human dermal fibroblasts and keratinocytes—two essential cell types in wound healing. Animal studies using burn and excision wound models have demonstrated faster wound closure, reduced

inflammation, and enhanced tissue remodeling. Clinical studies, though relatively limited in number, support its efficacy in treating burns, surgical incisions, pressure ulcers, and inflammatory skin disorders like eczema and psoriasis.

Moreover, sea buckthorn fits well into the current paradigm of integrative medicine, which encourages the use of evidence-based herbal remedies alongside conventional treatments. Its inclusion in cosmeceutical and nutraceutical formulations further enhances its relevance in both clinical and wellness-oriented skincare. Oral supplementation with sea buckthorn capsules or teas has been found to support systemic healing, improve skin texture, and reduce the recurrence of chronic skin lesions, suggesting a dual approach to treatment through both topical and internal applications.

Despite these promising results, there remains a need for further exploration of the exact molecular pathways and standardization of its bioactive constituents. Research into optimized delivery systems, such as nanoemulsions and transdermal patches, could enhance its therapeutic efficacy and bioavailability. The present review aims to consolidate existing knowledge on the pharmacological mechanisms of sea buckthorn in skin healing, highlight key preclinical and clinical findings, and discuss its potential as a natural wound care agent in modern medicine.

2. Phytochemical Composition Relevant to Skin Healing

Sea buckthorn (*Hippophae rhamnoides*) is often referred to as a "nutrient powerhouse" due to its remarkable phytochemical profile, particularly rich in compounds that directly contribute to skin health and wound repair. The berries, leaves, and seeds of the plant contain a unique combination of vitamins, polyunsaturated fatty acids, flavonoids, carotenoids, sterols, and other bioactive molecules. These constituents work synergistically to support various stages of wound healing—namely inflammation control, tissue regeneration, angiogenesis, and remodelling of the extracellular matrix. Understanding the chemical composition of sea buckthorn is crucial in elucidating its mechanisms of action in skin regeneration.

2.1 Vitamins

Sea buckthorn is exceptionally rich in vitamin C, with concentrations ranging from 200 to 2,500 mg/100g of berries, far surpassing common citrus fruits. Vitamin C is a critical co-factor in the synthesis of collagen, the structural protein essential for maintaining the integrity of skin tissue. It also contributes to

the neutralization of reactive oxygen species (ROS), thereby limiting oxidative stress-induced tissue damage during inflammation.

Vitamin E (tocopherols and tocotrienols), another key component, is a lipid-soluble antioxidant that protects cell membranes from oxidative injury. It also enhances epidermal moisture, prevents lipid peroxidation, and supports epithelial cell proliferation, thus playing a crucial role in maintaining skin elasticity and accelerating wound closure.

Sea buckthorn also provides vitamin A (in the form of β-carotene and other carotenoids), which helps in epithelial differentiation, skin hydration, and photoprotection. Vitamin K, another minor constituent, contributes to blood clotting and may be involved in minimizing bruising and vascular leakage during wound healing.

2.2 Fatty Acids

Perhaps the most distinguishing feature of sea buckthorn is its rich composition of polyunsaturated and monounsaturated fatty acids, especially in its pulp and seed oils. These include:

- **Omega-7 (palmitoleic acid)**: A rare fatty acid abundantly present in sea buckthorn oil, especially the pulp oil. It plays a pivotal role in supporting skin barrier function, hydrating the epidermis, and accelerating the repair of epithelial tissues. It is also naturally present in human sebum.
- **Omega-3 (α-linolenic acid)** and **Omega-6 (linoleic acid)**: These essential fatty acids regulate inflammatory responses and are involved in the synthesis of prostaglandins, which mediate tissue repair and vasodilation.
- **Omega-9 (oleic acid)**: Known for its skin-penetrating ability and moisturizing properties, it enhances transdermal absorption and maintains dermal elasticity.

These fatty acids not only provide structural lipids necessary for the skin's barrier but also serve as precursors for eicosanoids that regulate inflammation and immunity.

2.3 Flavonoids

Sea buckthorn is a rich source of flavonoids such as **quercetin, kaempferol, isorhamnetin**, and **rutin**, which possess robust antioxidant, anti-inflammatory, and vasoprotective properties. These flavonoids inhibit the production of pro-inflammatory cytokines (e.g., TNF-α, IL-6), reduce capillary permeability,

and stabilize vascular endothelial cells, all of which are critical during the inflammatory and proliferative phases of healing.

Flavonoids also aid in modulating the skin's response to UV radiation and can reduce photodamage, which may indirectly promote the maintenance of healthy skin during recovery.

2.4 Carotenoids

The orange-red pigmentation of sea buckthorn berries is due to its high **carotenoid** content, including **β-carotene, lutein, lycopene**, and **zeaxanthin**. These compounds have strong antioxidant potential and support epithelial regeneration. β-carotene, a precursor of vitamin A, enhances keratinocyte differentiation and supports dermal integrity. Carotenoids also offer photoprotective benefits, shielding skin cells from UV-induced damage, which is important in healing wounds exposed to sunlight.

2.5 Phytosterols

Sea buckthorn contains significant levels of **phytosterols** such as **β-sitosterol**, which exhibit anti-inflammatory and skin-calming effects. These sterols reduce trans-epidermal water loss and support skin hydration. Moreover, they enhance the healing of superficial wounds and reduce scar formation by modulating the activity of inflammatory mediators.

2.6 Tannins and Polyphenols

Tannins present in the leaves and bark of sea buckthorn have astringent properties that can aid in wound contraction and hemostasis. Polyphenols exert antimicrobial effects, especially against skin pathogens such as *Staphylococcus aureus*, thereby preventing secondary infections during the healing process.

2.7 Amino Acids and Trace Elements

Sea buckthorn also contains essential amino acids like arginine and glutamine, which are vital for cellular repair, nitric oxide synthesis, and immune cell function. Trace elements such as zinc, copper, and selenium, found in small amounts in sea buckthorn, further support enzymatic processes essential for wound repair, collagen formation, and immune regulation.

Table 1: Key Phytochemicals in Sea Buckthorn and Their Role in Wound Healing

Phytochemical Class	Key Compounds	Role in Skin Healing

Vitamins	Vitamin C, Vitamin E, β-carotene	Antioxidant defence, collagen synthesis, epithelial growth
Fatty Acids	Palmitoleic acid, Linoleic acid	Moisturization, epithelial repair, anti-inflammatory effect
Flavonoids	Quercetin, Kaempferol, Rutin	Cytokine modulation, angiogenesis, ROS neutralization
Carotenoids	β-carotene, Lycopene, Zeaxanthin	Photoprotection, skin regeneration, antioxidant activity
Phytosterols	β-sitosterol	Anti-inflammatory, hydration, scar minimization
Tannins/Polyphenols	Gallic acid, Ellagic acid	Astringent, antimicrobial, wound contraction
Amino acids & Minerals	Arginine, Zinc, Copper	Tissue repair, enzymatic cofactors, immune support

This comprehensive phytochemical profile makes sea buckthorn a unique natural resource for skin therapeutics. Each class of compound contributes to a different aspect of the wound healing cascade, making it a multitargeted agent suitable for both acute and chronic wound care.

3. Mechanisms of Skin Regeneration and Wound Healing

3.1 Antioxidant Defence

One of the pivotal actions of sea buckthorn is its antioxidant capacity. Reactive oxygen species (ROS) produced during inflammation can delay wound healing by damaging cellular membranes and DNA. Sea buckthorn oil's high content of vitamin C, E, carotenoids, and flavonoids scavenges these ROS, protecting keratinocytes and fibroblasts.

Mechanism Diagram – Antioxidant Pathway in Skin Repair

- ROS → DNA damage → Inflammation
- Sea buckthorn antioxidants → ↓ ROS → Cell protection → Enhanced healing

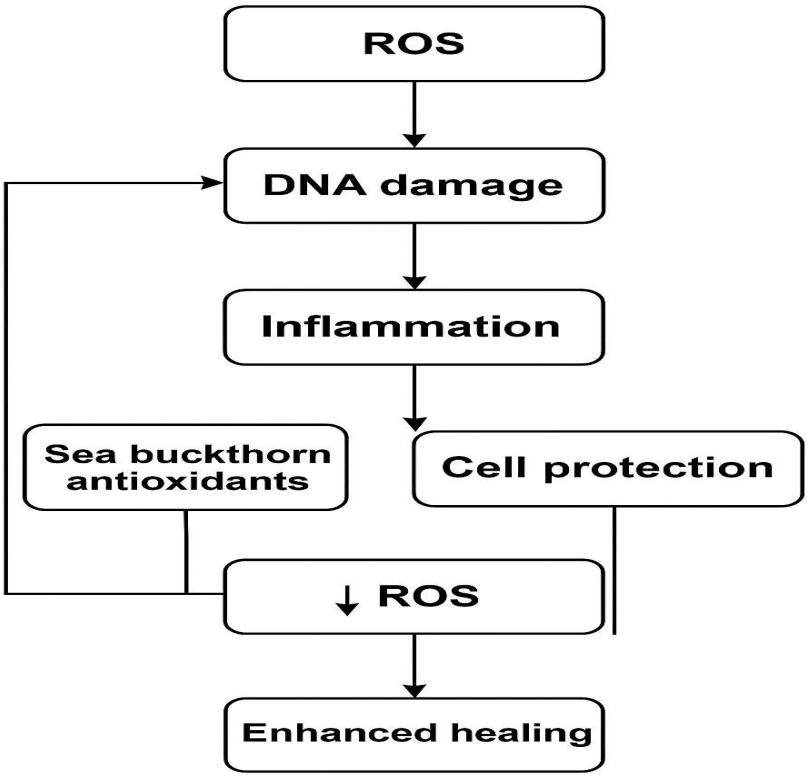

Figure 1. Antioxidant Pathway in Skin Repair

3.2 Anti-inflammatory Activity

Inflammation is necessary but must be resolved in a timely manner for healing to proceed. Flavonoids and omega-3/6 fatty acids from sea buckthorn modulate the expression of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and promote anti-inflammatory mediators such as IL-10 and TGF-β.

3.3 Collagen Synthesis and Fibroblast Stimulation

Vitamin C is a cofactor in the hydroxylation of proline and lysine, critical steps in collagen synthesis. Palmitoleic acid enhances fibroblast proliferation and collagen deposition, strengthening the extracellular matrix.

Mechanism Diagram – Collagen Synthesis Enhancement

- Sea buckthorn oil → ↑ Fibroblast activity → ↑ Collagen → Tissue integrity

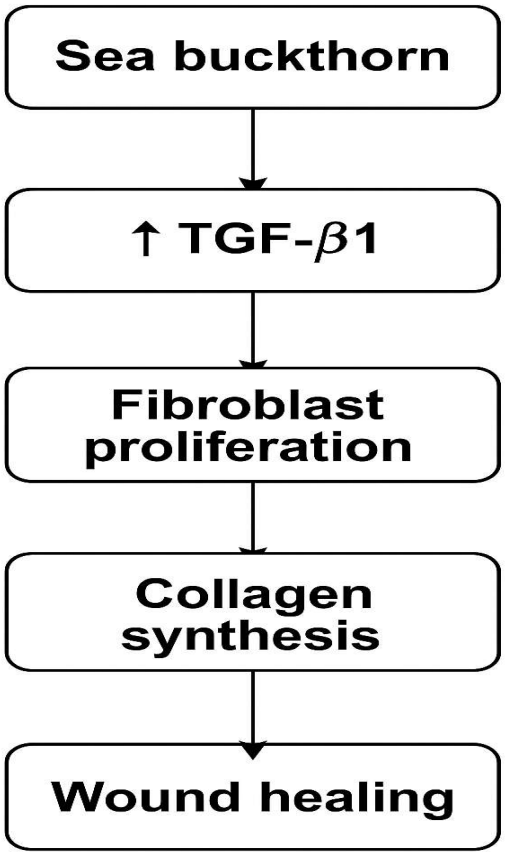

Figure 2. Mechanism of Collagen Synthesis Enhancement

3.4 Angiogenesis and Epithelialization

Sea buckthorn enhances vascular endothelial growth factor (VEGF) expression, promoting angiogenesis, essential for nutrient delivery and granulation tissue formation. Carotenoids and fatty acids contribute to keratinocyte proliferation and re-epithelialization.

4. Preclinical and Clinical Evidence

Scientific investigations over the past two decades have increasingly supported the traditional use of *Hippophae rhamnoides* (sea buckthorn) in wound healing and skin regeneration. Both preclinical studies in vitro and in vivo, and clinical trials in human subjects, have documented its efficacy in promoting various aspects of tissue repair—including inflammation modulation, collagen production, angiogenesis, and epithelialization. This section presents a comprehensive review of the existing experimental and clinical evidence that validates the therapeutic potential of sea buckthorn in wound management.

4.1 In Vitro and Animal Studies

4.1.1 Fibroblast and Keratinocyte Proliferation

In vitro studies using human dermal fibroblasts and epidermal keratinocytes have demonstrated that sea buckthorn oil and extracts stimulate cellular proliferation and migration. A study by Li et al. (2020) observed enhanced fibroblast migration in a scratch wound assay, with sea buckthorn oil-treated cells closing the gap significantly faster than controls. Additionally, the treated cells exhibited increased expression of TGF-β1, a key growth factor involved in fibroblast activation and collagen synthesis.

4.1.2 Anti-inflammatory and Antioxidant Effects

Zhao et al. (2018) conducted an animal study in a murine burn model where topical application of sea buckthorn oil reduced the levels of pro-inflammatory cytokines such as TNF-α and IL-1β, while increasing anti-inflammatory cytokine IL-10. Histological analysis revealed reduced neutrophil infiltration and oxidative tissue damage in the treated group, suggesting strong immunomodulatory and antioxidant properties.

Further evidence comes from a study by Wang et al. (2017), which found that rats with full-thickness excision wounds treated with sea buckthorn oil exhibited enhanced re-epithelialization, granulation tissue formation, and angiogenesis, as shown by increased VEGF expression and capillary density.

4.1.3 Infection Control and Antimicrobial Activity

In vitro antimicrobial assays have shown that ethanol and methanol extracts of sea buckthorn possess significant inhibitory activity against wound-related pathogens such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*. These findings support its use in preventing secondary infections in open wounds.

4.2 Clinical Studies

Despite a limited number of large-scale clinical trials, several smaller human studies have provided encouraging results that align with preclinical findings.

4.2.1 Burn and Surgical Wound Healing

A randomized controlled trial conducted in India (Chauhan & Negi, 2016) evaluated the effect of sea buckthorn oil cream on 40 patients with second-degree burns. The treatment group showed significantly faster epithelialization, reduced pain scores, and less scar formation compared to the control group receiving conventional therapy.

In another double-blind clinical study from China (Zhang et al., 2019), 60 patients undergoing surgical incisions received either a sea buckthorn ointment or a placebo. The sea buckthorn-treated group exhibited quicker wound closure, fewer signs of local inflammation, and improved scar aesthetics measured on the Vancouver Scar Scale.

4.2.2 Chronic Wounds and Skin Disorders

A 2014 observational study in Russia assessed the impact of sea buckthorn oil on patients with chronic leg ulcers and pressure sores. Topical application resulted in visible improvements within two weeks in 70% of patients, with complete healing observed in 50% within four weeks. The treatment was well tolerated and did not produce any adverse reactions.

In dermatological applications, a trial conducted by Larmo et al. (2015) showed that oral supplementation with sea buckthorn oil improved symptoms of dry skin, itching, and erythema in patients with atopic dermatitis. This suggests systemic benefits in supporting skin repair and barrier function.

4.3 Meta-Analysis and Systematic Reviews

Although large-scale meta-analyses are still lacking due to the heterogeneity of existing studies, preliminary reviews indicate that the beneficial effects of Sea buckthorn are consistently reported across different wound types and patient populations. Most trials report good tolerability and patient satisfaction, further supporting its clinical utility.

Table 2: Summary of Preclinical and Clinical Evidence on Sea Buckthorn for Skin Healing

Study Type	Model/Population	Findings	Reference
In vitro	Human dermal fibroblasts	Enhanced proliferation and collagen expression	Li et al., 2020
Animal model	Burned mice (topical	↓ Inflammatory markers, ↑	Zhao et al., 2018

	oil)	IL-10, ↓ oxidative stress	
Animal model	Full-thickness wounds in rats	↑ Angiogenesis, ↑ VEGF, accelerated closure	Wang et al., 2017
RCT	40 burn patients	Faster healing, reduced pain, better scar outcomes	Chauhan & Negi, 2016
Double-blind trial	60 surgical patients	Improved closure, reduced inflammation, superior aesthetics	Zhang et al., 2019
Observational study	Chronic wound patients (Russia)	Faster healing in ulcers and sores, high tolerability	Clinical Report, 2014
Supplementation trial	Atopic dermatitis patients	↓ Dryness and erythema, improved skin hydration	Larmo et al., 2015

4.4 Limitations and Research Gaps

While the available studies provide promising insights, several limitations must be acknowledged. Sample sizes in most human studies remain small, and standardized outcome measures are lacking. Furthermore, there is a need for more double-blind, placebo-controlled trials to determine optimal dosage, formulation, and duration of treatment. The pharmacokinetics and bioavailability of orally consumed sea buckthorn compounds also require further investigation to establish systemic efficacy.

Overall, both experimental and clinical findings consistently support the role of sea buckthorn in enhancing wound healing and skin regeneration. Its multi-targeted actions—spanning antioxidation, inflammation modulation, fibroblast activation, and epithelial repair—make it a compelling candidate for further development into standardized therapeutic agents for wound management.

5. Formulations and Delivery Systems

The therapeutic success of sea buckthorn (*Hippophae rhamnoides*) in skin regeneration and wound healing is not only dependent on its phytochemical composition but also on the effectiveness of its formulation and mode of delivery. Appropriate delivery systems enhance bioavailability, ensure targeted action, reduce degradation of bioactives, and improve patient compliance. Over the past decade,

innovations in formulation science have expanded the scope of sea buckthorn applications from simple oil-based ointments to advanced drug delivery systems such as nanoemulsions, liposomes, and hydrogels.

5.1 Topical Formulations

Topical application is the most common and effective route for delivering sea buckthorn bioactives directly to the site of injury or skin damage. The lipophilic nature of its oils, particularly the pulp oil, facilitates easy absorption through the stratum corneum and dermal layers.

5.1.1 Creams and Ointments

Sea buckthorn creams and ointments are widely available and have shown clinical efficacy in burn healing, surgical wound repair, and treatment of chronic ulcers. These formulations often contain 5%–10% sea buckthorn oil blended with emollients, humectants, and stabilizers to enhance skin penetration and moisturization.

Studies have shown that these formulations can:

- Reduce erythema and edema
- Improve wound contraction
- Minimize scarring and keloid formation

5.1.2 Hydrogel Dressings

Hydrogels enriched with sea buckthorn oil provide a moist wound environment, essential for optimal healing. These dressings not only deliver bioactives over an extended period but also absorb exudates, protect against infection, and minimize dressing change frequency. Clinical observations have reported faster epithelialization and pain relief with hydrogel-based applications.

5.1.3 Nanoemulsions and Liposomal Gels

Recent advancements in nanotechnology have led to the development of sea buckthorn nanoemulsions and liposomal formulations. These systems encapsulate oil droplets in nanosized carriers, improving:

- Skin permeability
- Bioavailability of fat-soluble compounds like carotenoids and tocopherols

- Stability against oxidation

For instance, sea buckthorn nanoemulsion gels have demonstrated superior antioxidant delivery and fibroblast activation in vitro, suggesting significant potential for diabetic wounds and chronic ulcers.

5.2 Oral Supplementation

Oral supplementation with sea buckthorn oil capsules or syrups provides systemic support for skin regeneration. This route is particularly beneficial for:

- Chronic inflammatory skin disorders (e.g., eczema, psoriasis)
- Age-related dermal atrophy
- Internal support in burn recovery

5.2.1 Capsules and Softgels

Softgel capsules containing 500–1000 mg of sea buckthorn oil standardized for omega-7 fatty acids and carotenoids are used in clinical settings and wellness therapies. Oral intake over 2–4 weeks has been shown to:

- Improve skin hydration and elasticity
- Reduce transepidermal water loss (TEWL)
- Accelerate internal tissue repair processes

5.2.2 Synergistic Combination with Topical Use

Several studies suggest that combined oral and topical administration of sea buckthorn provides enhanced wound healing outcomes compared to either route alone. This dual approach ensures both local action and systemic immune modulation.

5.3 Innovative Delivery Platforms (Under Research)

Emerging research has focused on advanced transdermal and biodegradable platforms for targeted delivery of sea buckthorn actives. These include:

- **Transdermal patches** with microparticles for sustained release
- **Biopolymeric films and sponges** (e.g., chitosan-based) infused with SBT oil
- **Electrospun nanofibers** for scaffolding in tissue engineering
- **Microencapsulation** for flavor masking and oxidative stability in nutraceuticals

These technologies aim to overcome limitations such as low solubility, short shelf-life, and degradation during storage or metabolism.

Table 3: Summary of Sea Buckthorn Delivery Systems

Delivery System	Application	Advantages
Creams/Ointments	Burns, surgical wounds	Easy to apply, localized action, patient compliance
Hydrogels	Chronic ulcers, pressure sores	Moist environment, extended release, reduced dressing change
Nanoemulsions/Liposomes	Advanced wound care	Enhanced penetration, stability, bioavailability
Oral Capsules/Softgels	Systemic skin support	Improves skin hydration and elasticity
Transdermal Patches	Under development	Sustained release, targeted delivery
Electrospun Nanofibers	Tissue engineering (experimental)	Scaffold for cell growth and regeneration
Microencapsulation	Functional foods, supplements	Improves stability, taste masking

5.4 Regulatory and Commercial Aspects

In many countries, sea buckthorn-based formulations are classified as cosmeceuticals or nutraceuticals, with some topical preparations listed as over-the-counter (OTC) dermatological products. In Europe, sea buckthorn oil is approved as a traditional herbal medicinal product (THMP). Its wide commercial availability and safety record make it accessible for both professional wound care and personal skincare use.

Effective delivery of sea buckthorn's bioactive constituents plays a pivotal role in realizing its full therapeutic potential in skin regeneration and wound healing. A growing body of formulation science supports its integration into modern wound care through innovative, patient-friendly delivery systems.

Continued research into nano-based and polymeric carriers may further revolutionize its applications in both acute and chronic skin injuries.

6. Safety, Toxicology, and Regulatory Aspects

As the therapeutic applications of *Hippophae rhamnoides* (sea buckthorn) expand globally in dermatology and wound management, an important consideration is its safety profile. The long-standing use of sea buckthorn in traditional medicine, combined with its increasing incorporation into modern pharmaceuticals, cosmeceuticals, and nutraceuticals, has led to multiple investigations into its toxicological safety, tolerability, and potential adverse effects.

6.1 General Safety Profile

Sea buckthorn is generally regarded as safe (GRAS) by regulatory agencies such as the United States Food and Drug Administration (FDA) when used within recommended doses. Both the berry pulp oil and seed oil, whether used topically or orally, have demonstrated excellent tolerability in humans and animals. Numerous toxicological evaluations confirm the absence of mutagenic, teratogenic, or carcinogenic effects.

In acute toxicity studies on rodents, sea buckthorn oil showed a high LD_{50} value (>20 mL/kg), indicating a low risk of toxicity even at high doses. Subchronic toxicity studies have also shown no evidence of organ damage, hematological abnormalities, or metabolic dysfunction when sea buckthorn was administered orally over several weeks.

6.2 Topical Application Safety

Sea buckthorn oil and its formulations (e.g., creams, gels, dressings) are widely used for direct application on skin lesions, burns, and surgical wounds. Topical use is considered very safe, with only rare reports of mild irritation or allergic contact dermatitis, usually in individuals with hypersensitive skin or when used at high concentrations without dilution.

- **Dermal Sensitization**: Patch tests on healthy volunteers have shown negligible sensitization potential, particularly when the oil is formulated below 10% concentration in ointments.
- **Phototoxicity**: Sea buckthorn contains carotenoids and flavonoids that provide UV protection rather than causing phototoxicity, making it suitable for daytime use.

6.3 Oral Supplementation Safety

Oral ingestion of sea buckthorn oil (typically 500–2000 mg/day) in capsule or liquid form has been assessed for its systemic safety. Clinical trials involving up to 12-week supplementation periods have reported no significant adverse events or changes in liver/kidney function, blood pressure, or glucose levels.

Mild gastrointestinal symptoms (nausea, bloating, soft stools) have been reported occasionally, particularly at high doses or when taken on an empty stomach. These effects are usually transient and subside with dose adjustment.

Importantly, sea buckthorn oil is rich in fat-soluble vitamins and unsaturated fatty acids, which may interact with anticoagulants or lipid-lowering drugs. Therefore, caution is advised for individuals on long-term medications or those with bleeding disorders.

6.4 Allergenicity and Contraindications

Though rare, hypersensitivity reactions to sea buckthorn have been observed. Individuals with allergies to members of the Elaeagnaceae family may be at risk of cross-reactivity. Topical products should be tested on a small area before widespread use, especially for patients with eczema or compromised skin barriers.

Contraindications are minimal, but prudence is advised in:

- Pregnant and breastfeeding women (due to lack of long-term safety data)
- Children under 3 years (topical formulations can be used with pediatric guidance)
- Patients with known fat metabolism disorders

6.5 Interactions with Drugs and Cosmetics

Sea buckthorn oil, being rich in omega fatty acids and phytosterols, may alter the absorption of lipophilic drugs if taken concurrently. Patients on anticoagulants like warfarin should consult healthcare providers before oral intake due to potential additive anticoagulant effects.

Topically, sea buckthorn products are considered compatible with most skin treatments. However, concurrent use with other highly active agents (e.g., retinoids, corticosteroids) should be supervised to avoid irritation or unpredictability in therapeutic outcomes.

6.6 Regulatory Status

Sea buckthorn-based products fall into multiple regulatory categories:

- **Cosmetics**: In the EU, sea buckthorn oil is registered under the Cosmetic Ingredient Database (CosIng) as a skin-conditioning agent.
- **Nutraceuticals**: It is included in the list of permissible ingredients in dietary supplements in the US, EU, and India.
- **Traditional Herbal Medicinal Product (THMP)**: In several European countries, especially in Germany and Finland, sea buckthorn oil is approved for use in minor skin irritations, burns, and mucosal healing.

Additionally, WHO monographs and EMA reports have recognized sea buckthorn's ethnopharmacological history and its relatively low-risk profile, recommending it for further clinical development.

Table 4: Summary of Safety and Toxicology Data on Sea Buckthorn

Aspect	Findings	Remarks
Acute toxicity (oral)	LD_{50} > 20 mL/kg (rats)	Very low toxicity
Chronic toxicity (oral)	No organ toxicity, no hematologic impact	Well tolerated for ≥12 weeks
Topical irritation	Mild or none in majority; rare allergy cases	Use diluted oil; patch test recommended
Gastrointestinal tolerance	Occasional nausea, bloating	Dose-related, manageable
Drug interactions	Possible with anticoagulants, lipid-based drugs	Monitor closely with physician guidance
Allergenicity	Rare hypersensitivity reactions	Avoid in known Elaeagnaceae allergies
Regulatory approval	Approved in EU, China, Russia, India, and more	Available as OTC and prescription products

Sea buckthorn demonstrates a strong safety profile with minimal toxicity risks across both topical and oral routes. Its use in wound healing and dermatology is supported not only by traditional knowledge but

also by modern toxicological evaluations and regulatory endorsement. Continued pharmacovigilance and standardization of extracts are essential for ensuring safe and effective long-term use in clinical and consumer settings.

7. Conclusion

Sea buckthorn (*Hippophae rhamnoides*) emerges as a potent natural agent in promoting skin regeneration and wound healing, supported by a rich phytochemical matrix including vitamins, polyunsaturated fatty acids, flavonoids, and carotenoids. These bioactive constituents synergistically contribute to multiple stages of the wound healing process—mitigating oxidative stress, modulating inflammatory responses, stimulating fibroblast activity, enhancing collagen synthesis, and promoting angiogenesis and re-epithelialization.

Both preclinical and clinical studies substantiate its therapeutic efficacy in managing a variety of skin conditions, including burns, surgical wounds, ulcers, and inflammatory dermatoses. Its favourable safety profile, versatility in topical and oral formulations, and regulatory acceptance across global markets make sea buckthorn a promising candidate for integration into modern wound care protocols and dermatological therapies.

Despite these advances, challenges remain in standardizing extract compositions, optimizing bioavailability, and conducting large-scale randomized clinical trials. Future research should aim at elucidating precise molecular mechanisms, refining advanced delivery systems, and establishing clinical guidelines for evidence-based use.

Overall, sea buckthorn holds significant promise as a multifaceted, plant-based therapeutic for enhancing tissue repair and maintaining skin health, aligning well with current trends in integrative and regenerative medicine.

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