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NEEM, ALOE VERA, AND TURMERIC: A REVIEW OF THEIR SYNERGISTIC POTENTIAL IN POLYHERBAL CREAMS FOR PSORIASIS SCAR MANAGEMENT

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ABSTRACT: Psoriasis, a chronic inflammatory skin condition, which leads to residual scarring to patients. Conventional treatments for these scars have limitations, driving interest in herbal remedies. This review examines the potential of Neem (*Azadirachta indica*), Aloe vera (*Aloe barbadensis* Miller), and Turmeric (*Curcuma longa*), individually and in combination, for managing psoriasis scars, particularly within polyherbal cream formulations. The review covers the phytochemical composition, pharmacological properties, clinical evidence, and mechanisms of action of these herbs, along with formulation considerations, safety profiles, and future research directions. Neem, Aloe vera, and Turmeric possess anti-inflammatory, wound-healing, and skin-regenerative properties. Combining them may offer synergistic benefits for improving psoriasis scar appearance. Further research is needed to validate these effects and develop standardized, effective, and safe polyherbal creams.

INTRODUCTION: Psoriasis a chronic inflammatory skin condition affecting 2-3% of the global population is characterized by the rapid accumulation of skin cells, leading to thick, silvery scales and itchy, dry, red patches. While various treatments can manage psoriasis symptoms, effectively addressing the residual scarring remains a challenge. These scars, which may present as post-inflammatory hyperpigmentation (PIH), textural irregularities, and atrophic or hypertrophic changes, can significantly affect a patient's well-being, including self-esteem, social interactions, and psychological health¹⁻². Traditional treatments for psoriasis scars include topical corticosteroids, retinoids, laser therapy, and dermabrasion.

However, these methods can have considerable side effects, such as skin irritation, thinning, and photosensitivity, and their effectiveness in completely resolving scars can vary. Additionally, the high cost and limited availability of some treatments can be a barrier for many patients³⁻⁴. There is a growing interest in using herbal remedies for various skin conditions, including psoriasis and its scarring. This is partly due to the perception that natural products are safer, more affordable, and have fewer adverse effects than synthetic drugs.

Among the medicinal plants investigated for dermatological benefits, Neem (*Azadirachta indica*), Aloe vera (*Aloe barbadensis* Miller), and Turmeric (*Curcuma longa*) are notable for their anti-inflammatory, wound-healing, and skin-regenerative properties⁵⁻⁶. This review provides a comprehensive overview of the potential of Neem, Aloe vera, and Turmeric, both individually and in combination, for managing psoriasis scars, with a focus on their incorporation into polyherbal cream formulations.

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It examines the phytochemical composition of these herbs, their pharmacological properties relevant to scar management, the available clinical evidence, and the potential mechanisms underlying their combined effects. Formulation considerations, safety profiles, and future research directions for developing effective and safe polyherbal creams for psoriasis scar management are also discussed⁷⁻⁸.

Psoriasis and Scar Formation:

Pathophysiology of Psoriasis: Psoriasis is a complex disease with multiple contributing factors, including a strong genetic component. Its development involves immune system dysregulation, notably the activation of T lymphocytes. These cells release pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-17 (IL-17), interleukin-22 (IL-22), and interferon-gamma (IFN- γ) (Nickoloff *et al.*, 2007). These cytokines are key drivers of keratinocyte hyperproliferation, the process that leads to the thickened plaques and scales characteristic of psoriasis⁹.

The precise triggers for immune system activation in psoriasis are not fully understood. However, several factors are believed to play a role. Specific genetic variations increase the likelihood of developing psoriasis. Triggers such as stress, infections, skin injuries, and certain medications can worsen psoriasis symptoms. Psoriasis is considered an autoimmune condition in which the immune system mistakenly targets the body's own tissues¹⁰. The interplay between genetic predisposition and environmental factors in psoriasis is complex and not fully elucidated.

Research suggests that in genetically susceptible individuals, various environmental triggers can activate immune cells, leading to a cascade of inflammatory events in the skin. These triggers can include infections (e.g., streptococcal throat infection), stress (both physical and psychological), skin trauma (known as the Koebner phenomenon), and certain medications (e.g., beta-blockers, lithium). The exact mechanisms by which these triggers initiate and perpetuate the psoriatic process are still under investigation, but they likely involve the activation of antigen-presenting cells, such as dendritic cells, which then stimulate T cells to produce pro-inflammatory cytokines¹¹⁻¹³.

Scar Formation in Psoriasis: Scarring is a natural part of skin repair after injury or inflammation. However, in chronic inflammatory conditions like psoriasis, sustained and dysregulated inflammation can disrupt the normal healing process, resulting in abnormal scars. Several factors contribute to scar formation in psoriasis. The ongoing inflammation in psoriasis lesions can damage the dermal extracellular matrix, which provides structural support to the skin. The deposition of collagen, a protein crucial for skin strength and elasticity, is disrupted in psoriasis. This disruption can lead to excessive collagen deposition (hypertrophic scars) or insufficient collagen deposition (atrophic scars). Matrix metalloproteinases (MMPs), enzymes that break down extracellular matrix components, are often elevated in psoriasis, contributing to tissue damage and scar formation. Various growth factors, such as transforming growth factor-beta (TGF- β), are involved in wound healing and scar formation. Their dysregulation in psoriasis can lead to abnormal scarring.

The process of scar formation is a complex and dynamic process that involves three overlapping phases: inflammation, proliferation, and remodeling. In psoriasis, the chronic inflammatory environment disrupts the normal progression of these phases, leading to the formation of abnormal scars. For example, prolonged inflammation can lead to excessive fibroblast activation and collagen deposition, resulting in hypertrophic scars. Conversely, inadequate collagen deposition or excessive matrix degradation can lead to atrophic scars. The balance between collagen synthesis and degradation is crucial for normal scar formation, and this balance is often disrupted in psoriasis due to the dysregulation of MMPs and their inhibitors¹⁴⁻¹⁶.

Psoriasis can lead to several types of scars, including post-inflammatory hyperpigmentation (PIH), a common complication of inflammatory skin conditions, including psoriasis. PIH involves skin darkening due to increased melanin production following inflammation and can persist for extended periods after active psoriasis lesions have healed. Psoriasis plaques can disrupt the skin's normal structure, leading to roughness, unevenness, and altered skin thickness.

Atrophic scars, which are depressions in the skin surface due to tissue loss, can result from severe inflammation or aggressive treatment in psoriasis. Hypertrophic scars are raised, thickened scars that stay within the original injury boundaries, while keloids extend beyond the original injury. While less common in psoriasis, they can occur, particularly in genetically predisposed individuals. It is important to differentiate between true scarring and the residual skin changes that are commonly observed after psoriasis lesions have resolved. While PIH and textural irregularities can be significant concerns for patients, they do not always represent true scarring in the pathological sense. True scarring involves permanent changes in the dermal architecture, with alterations in collagen organization and composition¹⁷⁻²¹.

Impact of Psoriasis Scars: Psoriasis scars can significantly affect a patient's well-being, influencing their physical, psychological, and social aspects. Visible scars, especially on the face or exposed body areas, can lead to emotional distress, causing feelings of self-consciousness, embarrassment, and shame, potentially leading to anxiety and depression. Scars can negatively impact self-image and confidence, reducing self-esteem. They can also lead to social stigma and discrimination, causing feelings of isolation. The emotional distress and social stigma associated with scars can hinder relationship formation, educational or career pursuits, and social participation. Additionally, scars can be itchy or painful, causing further distress and interfering with daily life. The impact of psoriasis scars on quality of life can be substantial and should not be underestimated. Patients with visible scars may experience significant psychological distress, which can affect their overall well-being and their ability to function in daily life. In some cases, the emotional burden of scarring can be as significant as the physical symptoms of psoriasis itself²²⁻²⁷.

In addition to psychological and social effects, psoriasis scars can have physical consequences. Scars can restrict skin movement, particularly over joints, leading to a limited range of motion. Some scars, like those from chronic inflammation, may slightly increase the risk of skin cancer. Therefore, effective management of psoriasis scars is important for both physical appearance and the

overall well-being of affected individuals. The development of effective treatments for psoriasis scars requires a comprehensive understanding of the complex interplay between the inflammatory processes that drive the disease and the wound-healing mechanisms that contribute to scar formation. A multi-faceted approach that addresses both the underlying inflammation and the abnormal healing processes is likely to be most effective in preventing and treating psoriasis scars²⁸⁻²⁹.

Individual Therapeutic Potential of Neem, Aloe Vera, and Turmeric:

Neem (*Azadirachta indica*):

Botanical Characteristics: Neem, or *Azadirachta indica*, is a rapidly growing evergreen tree native to the Indian subcontinent and other tropical areas. It belongs to the Meliaceae family and has long been used in traditional Ayurvedic medicine for various conditions, including skin diseases, infections, and inflammation. Neem is a versatile tree with a wide range of applications. In addition to its medicinal uses, Neem is also valued for its insecticidal properties, and it is used in agriculture to protect crops from pests. The tree is also a source of timber, and its leaves and bark are used in various other products³⁰.

Phytochemical Composition: Neem contains many bioactive compounds. Azadirachtin is a key tetranortriterpenoid with insecticidal, anti-inflammatory, and immunomodulatory properties. Nimbin and Nimbidin are terpenoids with anti-inflammatory, antifungal, and antibacterial activities. Quercetin, a flavonoid, has antioxidant and anti-inflammatory properties. β -Sitosterol is a plant sterol with anti-inflammatory and wound-healing properties. Neem oil contains fatty acids like oleic, linoleic, and palmitic acid, contribute to moisturizing and skin-barrier-enhancing effects. Other compounds found in Neem, such as tannins, polyphenols, and limonoids, also contribute to its therapeutic properties. The phytochemical composition of Neem is complex and varies depending on the part of the plant and the extraction method used. Researchers have identified hundreds of different compounds in Neem, and many of these compounds have been shown to have biological activity. The synergistic interactions between these various compounds are

thought to contribute to the overall therapeutic efficacy of Neem³¹⁻³².

Pharmacological Properties: Neem has several pharmacological activities relevant to managing psoriasis scars. Neem extracts and compounds can inhibit pro-inflammatory cytokines like TNF- α , IL-1 β , and IL-6, which are involved in psoriasis and scar formation. Neem also inhibits cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, which produce inflammatory mediators. It has broad-spectrum antimicrobial activity against bacteria, fungi, and viruses. This is important in psoriasis, where patients have a higher risk of secondary skin infections due to a compromised skin barrier. Neem can promote wound healing by stimulating collagen synthesis, increasing fibroblast proliferation, and enhancing angiogenesis. Additionally, Neem contains antioxidants that can scavenge free radicals and protect skin cells from oxidative damage, and it can modulate the immune system by suppressing T cell activation and reducing pro-inflammatory cytokines. The diverse pharmacological properties of Neem make it a valuable therapeutic agent for a wide range of conditions, including psoriasis and its associated complications³³⁻³⁴.

Anti-inflammatory Mechanisms: Neem's anti-inflammatory action is mediated through several mechanisms. It inhibits the activation of nuclear factor-kappa B (NF- κ B), a key transcription factor that regulates the expression of numerous pro-inflammatory genes. By inhibiting NF- κ B, Neem reduces the production of pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. Neem also modulates the activity of enzymes involved in the arachidonic acid pathway, such as cyclooxygenase (COX) and lipoxygenase (LOX), leading to a reduction in the synthesis of prostaglandins and leukotrienes, which are potent mediators of inflammation. Furthermore, Neem has been shown to enhance the production of anti-inflammatory cytokines, such as interleukin-10 (IL-10), which can help to dampen the inflammatory response.

Wound-healing Mechanisms: Neem promotes wound healing by stimulating various aspects of the healing process. It enhances the proliferation of fibroblasts, the cells responsible for synthesizing

collagen and other extracellular matrix components. Neem also increases the deposition of collagen at the wound site, providing structural support and strength to the healing tissue. In addition, Neem promotes angiogenesis, the formation of new blood vessels, which is essential for delivering oxygen and nutrients to the wound and for removing waste products. Neem also possesses antimicrobial properties, which can help to prevent infection at the wound site, a major impediment to healing.

Antimicrobial Mechanisms: Neem exhibits broad-spectrum antimicrobial activity against a variety of microorganisms, including bacteria, fungi, and viruses. This activity is attributed to the presence of various bioactive compounds, such as azadirachtin, nimbin, and nimbidin, which can disrupt the cell membranes of microorganisms, interfere with their metabolic processes, and inhibit their growth and replication. Neem's antimicrobial properties are particularly beneficial in the context of psoriasis, where patients often have a compromised skin barrier and are more susceptible to secondary infections.

Antioxidant Mechanisms: Neem contains a variety of antioxidant compounds, such as quercetin and other flavonoids, which can scavenge free radicals and protect cells from oxidative damage. Oxidative stress plays a significant role in the pathogenesis of many inflammatory diseases, including psoriasis, and antioxidants can help to mitigate the damaging effects of free radicals. By reducing oxidative stress, Neem may contribute to the overall health of the skin and promote the healing of wounds and scars³⁵⁻⁴⁰.

Clinical Evidence: Clinical studies have explored Neem's efficacy in treating psoriasis. One study found that a Neem oil-based cream reduced the severity of psoriasis symptoms, including erythema, scaling, and pruritus. Another study showed Neem extract was comparable to coal tar in treating psoriasis, with fewer side effects. While specific clinical studies on Neem for psoriasis scar management are limited, evidence from psoriasis treatment studies, along with Neem's wound-healing and anti-scarring properties, suggests its potential in formulations for reducing psoriasis scars.

Further research, including well-designed clinical trials specifically focused on the effects of Neem on psoriasis scars, is warranted to fully evaluate its therapeutic potential in this area. Studies should also investigate the optimal dosage, formulation, and duration of treatment for achieving the best results⁴¹⁻⁴³.

Aloe Vera (*Aloe barbadensis* Miller):

Botanical Characteristics: Aloe vera, or *Aloe barbadensis* Miller, is a succulent plant in the Asphodelaceae family. Native to the Arabian Peninsula, it is now grown globally for its medicinal and cosmetic uses. The gel from Aloe vera leaves is rich in bioactive compounds and has been used for centuries for skin conditions like burns, wounds, and inflammation. Aloe vera is a relatively easy plant to grow, and it is often cultivated in home gardens for its medicinal and cosmetic properties. The plant thrives in warm, sunny climates and requires well-drained soil⁴⁴.

Phytochemical Composition: Aloe vera gel contains many bioactive compounds. Acemannan is a major polysaccharide with immunomodulatory, antiviral, and wound-healing properties. Anthraquinones like aloin and emodin have anti-inflammatory, analgesic, and antimicrobial activities. Aloe vera gel contains enzymes like bradykinase, catalase, and superoxide dismutase, contributing to anti-inflammatory and antioxidant effects. Aloe vera provides vitamins A, C, and E, and minerals like zinc and selenium, which are important for skin health and wound healing. Other compounds found in Aloe vera include salicylic acid, amino acids, and sterols. The gel found within Aloe vera leaves is a complex mixture of polysaccharides, enzymes, vitamins, minerals, and other organic compounds. Acemannan, a long-chain polysaccharide, is one of the most abundant and biologically active components of Aloe vera gel. Other important constituents include anthraquinones, such as aloin and emodin, which have laxative and antimicrobial properties, and various enzymes, such as bradykinase, which has anti-inflammatory and analgesic effects⁴⁵⁻⁴⁶.

Pharmacological Properties: Aloe vera has several activities relevant to managing psoriasis scars. Aloe vera gel promotes wound healing by stimulating fibroblast proliferation, increasing

collagen synthesis, and enhancing extracellular matrix deposition. It also promotes angiogenesis. Aloe vera gel has anti-inflammatory effects by inhibiting pro-inflammatory cytokines like TNF- α and IL-1 β . It also inhibits COX enzymes, reducing prostaglandins. Aloe vera gel is a natural humectant, helping the skin retain moisture. This can improve skin hydration, reduce dryness and irritation, and enhance skin barrier function. Additionally, Aloe vera contains antioxidants that protect skin cells from free radical damage, and some studies suggest it may have anti-proliferative effects on keratinocytes. Aloe vera's diverse pharmacological properties make it a valuable therapeutic agent for a variety of skin conditions, including psoriasis and its associated scarring⁴⁷.

Wound-healing Mechanisms: Aloe vera promotes wound healing through a variety of mechanisms. It stimulates the proliferation of fibroblasts, the cells responsible for synthesizing collagen and other extracellular matrix components. Aloe vera also increases the synthesis of collagen, a fibrous protein that provides structural support and strength to the skin. In addition, Aloe vera enhances the deposition of extracellular matrix components, such as glycosaminoglycans, which play a crucial role in tissue repair and regeneration. Aloe vera also promotes angiogenesis, the formation of new blood vessels, which is essential for delivering oxygen and nutrients to the wound site and for removing waste products. Furthermore, Aloe vera possesses anti-inflammatory and antimicrobial properties, which can help to prevent infection and promote a favorable environment for healing.

Anti-inflammatory Mechanisms: Aloe vera exerts its anti-inflammatory effects through several pathways. It inhibits the production of pro-inflammatory cytokines, such as TNF- α , IL-1 β , and IL-6, which are key mediators of inflammation. Aloe vera also modulates the activity of enzymes involved in the arachidonic acid pathway, such as cyclooxygenase (COX), leading to a reduction in the synthesis of prostaglandins, which contribute to pain and inflammation. In addition, Aloe vera contains compounds, such as bradykinase, that have direct anti-inflammatory effects.

Moisturizing Mechanisms: Aloe vera gel is a natural humectant, meaning it has the ability to

attract and retain moisture. When applied to the skin, Aloe vera gel helps to increase the water content of the stratum corneum, the outermost layer of the epidermis, leading to improved hydration and reduced dryness. This moisturizing effect is particularly beneficial in the context of psoriasis, where the skin is often dry, scaly, and irritated. By improving skin hydration, Aloe vera can help to restore the skin barrier function and reduce the symptoms of psoriasis.

Anti-proliferative Effects: Some studies have suggested that Aloe vera may have anti-proliferative effects on keratinocytes, the cells that make up the epidermis. In psoriasis, keratinocytes proliferate at an abnormally rapid rate, leading to the formation of thick, scaly plaques. By inhibiting keratinocyte proliferation, Aloe vera may help to reduce the thickness and scaling of psoriatic lesions. However, further research is needed to fully elucidate the mechanisms and clinical significance of this effect⁴⁸⁻⁵⁰.

Clinical Evidence: Aloe vera's wound-healing properties are supported by clinical evidence. Numerous studies have shown its effectiveness in healing burns, surgical wounds, and chronic ulcers. A meta-analysis found Aloe vera gel significantly improved wound healing compared to conventional treatments. In psoriasis, some studies indicate Aloe vera gel can reduce symptoms like plaque thickness, erythema, and scaling. While specific studies on Aloe vera's effects on psoriasis scars are fewer, its wound-healing and skin-regenerative properties suggest it is a valuable component in formulations for improving scar appearance. Clinical studies have demonstrated the efficacy of Aloe vera in promoting wound healing in a variety of settings. Its use in the treatment of burns is particularly well-established, and Aloe vera is often used as a first-aid treatment for minor burns. Studies have also shown that Aloe vera can be effective in promoting the healing of chronic wounds, such as diabetic ulcers and venous leg ulcers⁵¹.

Turmeric (*Curcuma longa*):

Botanical Characteristics: Turmeric, or *Curcuma longa*, is a rhizomatous plant in the Zingiberaceae family. Native to South Asia, its rhizomes are used as a spice, coloring agent, and medicinal herb.

Turmeric has been used in traditional Ayurvedic and Chinese medicine for various conditions, including skin diseases, inflammation, and pain. Turmeric is a perennial plant that is typically grown for its rhizomes, which are underground stems that store nutrients. The rhizomes are harvested, dried, and ground into a powder, which is the form in which turmeric is most commonly used⁵².

Phytochemical Composition: Turmeric contains various bioactive compounds. Curcumin is the most well-known compound, a potent polyphenol with anti-inflammatory, antioxidant, and wound-healing properties. Turmerones are volatile oils with anti-inflammatory and antimicrobial activities. Turmeric contains polysaccharides with anti-inflammatory and immunomodulatory effects. Other compounds found in Turmeric include proteins, resins, and minerals. Curcumin is the most extensively studied component of turmeric, and it is responsible for many of the plant's therapeutic properties. However, turmeric also contains other curcuminoids, such as demethoxycurcumin and bisdemethoxycurcumin, as well as volatile oils, such as turmerone, ar-turmerone, and α -phellandrene, which also contribute to its biological activity⁵³.

Pharmacological Properties: Turmeric, especially curcumin, has several activities relevant to managing psoriasis scars. Curcumin inhibits various pro-inflammatory cytokines, including TNF- α , IL-1 β , IL-6, and IL-8. It also inhibits key enzymes like COX-2 and NF- κ B. Curcumin promotes wound healing by stimulating collagen synthesis, enhancing fibroblast proliferation, and promoting angiogenesis. Curcumin scavenges free radicals and protects skin cells from oxidative damage. It can also inhibit keratinocyte proliferation and melanin synthesis, which can help reduce hyperpigmentation in psoriasis scars. Turmeric, and particularly curcumin, exhibits a wide range of pharmacological activities that are relevant to the management of psoriasis and its associated scarring⁵⁴.

Anti-inflammatory Mechanisms: Curcumin is a potent inhibitor of NF- κ B, a master regulator of inflammation. By inhibiting NF- κ B activation, curcumin suppresses the expression of numerous pro-inflammatory genes, including those encoding

cytokines (e.g., TNF- α , IL-1 β , IL-6), chemokines, and adhesion molecules. Curcumin also modulates other signaling pathways involved in inflammation, such as the mitogen-activated protein kinase (MAPK) pathway and the Janus kinase/signal transducer and activator of transcription (JAK-STAT) pathway. In addition, curcumin can inhibit the activity of enzymes involved in the arachidonic acid pathway, such as cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), leading to a reduction in the synthesis of prostaglandins and leukotrienes, which are potent mediators of inflammation.

Wound-healing mechanisms: Curcumin promotes wound healing by stimulating several key processes. It enhances the proliferation and migration of fibroblasts, the cells responsible for synthesizing collagen and other extracellular matrix components. Curcumin also increases the deposition of collagen at the wound site, providing structural support and strength to the healing tissue. Furthermore, curcumin promotes angiogenesis, the formation of new blood vessels, which is essential for delivering oxygen and nutrients to the wound and for removing waste products. Curcumin also possesses antioxidant and antimicrobial properties, which can help to create a favorable environment for healing.

Antioxidant Mechanisms: Curcumin is a potent antioxidant that can scavenge a variety of free radicals, including reactive oxygen species (ROS) and reactive nitrogen species (RNS). Curcumin also enhances the activity of endogenous antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, providing further protection against oxidative stress. Oxidative stress plays a significant role in the pathogenesis of many inflammatory diseases, including psoriasis, and curcumin's antioxidant properties can help to mitigate the damaging effects of free radicals.

Anti-pigmentation Mechanisms: Curcumin has been shown to inhibit melanin synthesis, the process responsible for skin pigmentation. Curcumin downregulates the activity of tyrosinase, a key enzyme involved in the melanogenesis pathway. By inhibiting tyrosinase, curcumin can reduce the production of melanin, leading to a

lightening of the skin. This effect is particularly relevant in the context of post-inflammatory hyperpigmentation (PIH), a common complication of psoriasis that can contribute to scarring.⁵⁵⁻⁵⁶

Clinical Evidence: The therapeutic effects of Turmeric, particularly curcumin, have been shown in clinical studies. Studies show oral curcumin supplementation can improve psoriasis symptoms (Hung *et al.*, 2015). Topical curcumin formulations are also effective in managing psoriasis symptoms (Tu *et al.*, 2012). Clinical trials have demonstrated curcumin's efficacy in promoting wound healing and reducing scar formation. This evidence suggests that Turmeric is a promising candidate for formulations aimed at managing psoriasis scars. However, despite its numerous beneficial properties, curcumin has poor bioavailability, meaning that it is not easily absorbed into the bloodstream when administered orally. This limitation has led to the development of various strategies to improve curcumin bioavailability, such as the use of nanoparticles, liposomes, and other drug delivery systems. Topical application of curcumin, as in the case of polyherbal creams, can bypass some of these bioavailability issues, but formulation strategies are still needed to enhance its⁵⁷.

Synergistic Potential of Neem, Aloe Vera, and Turmeric: Combining Neem, Aloe vera, and Turmeric in a polyherbal cream may offer synergistic effects, enhancing their therapeutic potential for psoriasis scars. Synergism, where the combined effect of multiple substances is greater than the sum of their individual effects, can occur through various mechanisms in herbal medicine. Different compounds can act on various molecular targets. One herb may improve the absorption, distribution, metabolism, or excretion of another. Compounds can affect enzymes involved in inflammation, wound healing, or melanin synthesis. Additionally, one herb may protect against another's potential toxicity. Combining Neem, Aloe vera, and Turmeric may amplify their individual properties. The concept of synergism is a fundamental principle in traditional herbal medicine, where combinations of herbs are often used to achieve therapeutic effects that are greater than those of the individual herbs. This approach is based on the idea that the complex mixture of

phytochemicals in different herbs can interact with each other in beneficial ways, leading to enhanced efficacy and reduced toxicity compared to the use of single herbs⁵⁸.

Mechanisms of Synergistic Action: Several potential mechanisms may contribute to the synergistic action of Neem, Aloe vera, and Turmeric in managing psoriasis scars. Neem, Aloe vera, and Turmeric have anti-inflammatory properties but act through different pathways; combining them targets a broader range of inflammatory mediators. These herbs promote wound healing through different mechanisms, and their combination may enhance this process. Aloe vera moisturizes, and Neem oil improves the skin barrier; combined, they may synergistically improve skin hydration and barrier function. Turmeric and Aloe vera have skin-lightening properties, and Neem's anti-inflammatory effects can also reduce inflammation-triggered hyperpigmentation. Combining these herbs may provide a synergistic effect in preventing secondary infections⁵⁹.

Preclinical and Clinical Evidence of Synergism: While individual effects are well-supported, specific research on the synergistic effects of Neem, Aloe vera, and Turmeric in psoriasis scar management is limited. However, some studies suggest potential synergism. Some preclinical studies suggest combinations of these herbs can enhance wound healing in animal models. Research indicates combinations of anti-inflammatory herbs can have a greater effect on inflammatory mediators. Traditional use in Ayurvedic medicine suggests synergistic effects. Further research is needed to confirm their synergistic effects, including optimal ratios, interaction mechanisms, and long-term efficacy and safety⁶⁰.

Formulation Considerations for Polyherbal Creams: Developing a polyherbal cream with these herbs for psoriasis scar management requires careful formulation. Different extraction methods yield varying compositions of bioactive compounds. Standardization ensures consistent quality and efficacy. Extracts must be compatible with each other and the cream base. The cream base should be non-irritating, moisturizing, and compatible with extracts. Penetration enhancers can

increase the absorption of active compounds. The formulation should maintain its integrity over time. Preservatives prevent microbial growth. The pH should be compatible with skin's natural pH. The viscosity should allow for easy application. If extracts are solid particles, they should be small. Packaging should protect the cream and be convenient for use⁶¹⁻⁶².

Safety Profile and Potential Adverse Effects: Neem, Aloe vera, and Turmeric are generally safe for topical use, but some may experience allergic reactions or skin irritation. Some may be allergic to Neem, particularly to other plants in the Meliaceae family. Aloe Vera is generally well-tolerated, but prolonged use may cause irritation or allergies. Turmeric may cause skin irritation or staining with high concentrations or prolonged use.

Systemic absorption with topical application is generally low, but potential systemic effects, especially with long-term use, should be considered. Ingestion of Neem should be avoided. When using Aloe Vera, only the gel should be used to avoid latex contamination. With Turmeric, potential systemic effects and drug interactions, especially with long-term use, should be considered. Safety testing is crucial to ensure the final product is safe⁶³⁻⁶⁴.

Future Research Directions: Further research is needed to identify optimal ratios of the herbs, investigate mechanisms of synergism, develop standardized extracts, evaluate different formulations, and conduct preclinical and clinical studies. It is also necessary to investigate long-term effects and conduct cost-effectiveness analyses. Addressing these gaps can lead to more effective and safe polyherbal creams.

CONCLUSION: Psoriasis scars can affect quality of life. Herbal remedies like Neem, Aloe vera, and Turmeric show promise due to their anti-inflammatory, wound-healing, and skin-regenerative properties. Combining these herbs in a polyherbal cream may offer synergistic benefits. While more research is needed, current evidence suggests these herbs can be valuable in topical formulations for improving psoriasis scar appearance. Further research and development of standardized, well-formulated creams may provide

a safe and effective treatment option for individuals with this condition.

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