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POLYHERBAL CREAM FOR PSORIATIC SKIN UTILIZING *CITRUS SINENSIS* AND *LINUM USITATISSIMUM* OIL: A COMPREHENSIVE REVIEW

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Keywords:

Polyherbal cream, *Citrus sinensis*, *Linum usitatissimum*, Inflammation, Keratinocyte proliferation, Topical formulation

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ABSTRACT: Psoriasis is a chronic inflammatory skin disease characterized by hyperproliferation of keratinocytes, resulting in scaly, erythematous plaques. Conventional treatments often involve corticosteroids, retinoids, and immunosuppressants, which can have significant side effects and limited long-term efficacy. There is a growing interest in exploring complementary and alternative therapies, particularly those derived from natural sources, due to their potential for better tolerability and multifaceted mechanisms of action. This review article aims to provide a comprehensive overview of the potential of a polyherbal cream formulated with *Citrus sinensis* (sweet orange) peel extract and *Linum usitatissimum* (flaxseed) oil for the management of psoriatic skin. We will delve into the individual pharmacological properties of these natural ingredients, their traditional uses in skin disorders, and the scientific evidence supporting their efficacy in addressing the key pathological features of psoriasis. Furthermore, the formulation aspects of topical creams, the potential synergistic effects of combining these two ingredients, and the future perspectives for developing a safe and effective polyherbal treatment for psoriasis will be discussed.

INTRODUCTION: Psoriasis is a prevalent, chronic, immune-mediated inflammatory skin disorder affecting approximately 2-3% of the global population [1]. It manifests as well-demarcated, erythematous plaques covered with silvery scales, primarily on the scalp, elbows, knees, and lower back. The underlying pathophysiology involves a complex interplay of genetic predisposition, immune system dysregulation, and environmental triggers, leading to hyperproliferation of keratinocytes in the epidermis and infiltration of inflammatory cells in the dermis [2].

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The clinical presentation of psoriasis varies widely, ranging from localized mild disease to extensive, debilitating forms. Common subtypes include plaque psoriasis (psoriasis vulgaris), guttate psoriasis, inverse psoriasis, pustular psoriasis, and erythrodermic psoriasis [3]. Psoriasis not only affects the skin but can also be associated with significant comorbidities such as psoriatic arthritis, cardiovascular disease, metabolic syndrome, anxiety, and depression, impacting the overall quality of life of affected individuals [4].

Conventional treatments for psoriasis aim to control inflammation, reduce keratinocyte hyperproliferation, and alleviate symptoms. Topical therapies, including corticosteroids, vitamin D analogues, retinoids, and calcineurin inhibitors, are typically the first-line treatment for mild to moderate psoriasis [5]. Systemic therapies, such as methotrexate, cyclosporine, acitretin, and biologic agents targeting specific immune mediators (e.g.,

TNF-α, IL-17, IL-23), are reserved for more severe or recalcitrant cases [6]. While these treatments can be effective in managing psoriasis, they are often associated with significant side effects, require long-term use, and may lose efficacy over time. Moreover, access to expensive biologic therapies can be limited in many regions.

Given the chronic nature of psoriasis and the limitations of conventional treatments, there is a growing interest in exploring complementary and alternative medicine (CAM) approaches, particularly those utilizing natural products. Herbal remedies have been used for centuries to treat various skin conditions, and their potential for providing safer and more sustainable therapeutic options for psoriasis is being increasingly investigated [7]. Polyherbal formulations, which combine the therapeutic properties of multiple medicinal plants, are gaining popularity due to their potential for synergistic effects, broader spectrum of activity, and reduced risk of individual herb-related toxicity [8]. This review focuses on the potential of a polyherbal cream formulated with *Citrus sinensis* peel extract and *Linum usitatissimum* oil for the management of psoriatic skin. *Citrus sinensis* (L.) Osbeck, commonly known as sweet orange, is widely cultivated for its fruit, and its peel is a rich source of bioactive compounds. *Linum usitatissimum* L., or flaxseed, is an important oilseed crop with significant nutritional and medicinal value due to its high content of omega-3 fatty acids. We will explore the individual pharmacological properties of these ingredients, their relevance to the pathophysiology of psoriasis, and the rationale for their combination in a topical formulation.

***Citrus sinensis* (Sweet Orange) Peel Extract:**

Botanical Description and Traditional Uses: *Citrus sinensis* belongs to the family Rutaceae and is believed to have originated in Southeast Asia. Sweet orange is now cultivated in tropical and subtropical regions worldwide. The fruit peel, often considered a waste product of the citrus processing industry, is a rich source of various bioactive compounds, including flavonoids, phenolic acids, essential oils, and carotenoids [9]. In traditional medicine systems, different parts of the *Citrus sinensis* plant, including the peel, have been used for their therapeutic properties.

The peel has been traditionally employed for its digestive, carminative, anti-inflammatory, and antiseptic effects [10]. Topically, orange peel preparations have been used for skin brightening, wound healing, and treatment of minor skin irritations [11].

Phytochemical Constituents: The major bioactive constituents of *Citrus sinensis* peel include:

Flavonoids: Hesperidin, hesperetin, naringin, narirutin, and tangeretin are the predominant flavonoids found in sweet orange peel. Hesperidin, in particular, is present in high concentrations and has been extensively studied for its pharmacological activities [12].

Phenolic Acids: Ferulic acid, caffeic acid, and gallic acid are among the phenolic acids identified in orange peel extract, known for their antioxidant and anti-inflammatory properties [13].

Essential Oils: Limonene is the most abundant component of sweet orange peel essential oil, contributing to its characteristic aroma and exhibiting various biological activities [14]. Other minor components include myrcene, α-pinene, and β-pinene.

Carotenoids: β-Carotene, lutein, and zeaxanthin are present in orange peel and contribute to its antioxidant potential [15].

Pharmacological Properties Relevant to Psoriasis: Several *in-vitro* and *in -vivo* studies have demonstrated the pharmacological properties of *Citrus sinensis* peel extract and its constituents that are relevant to the management of psoriasis:

Anti-inflammatory Activity: Flavonoids like hesperidin have shown significant anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, and IL-8 [16]. These cytokines play a crucial role in the pathogenesis of psoriasis, driving keratinocyte hyperproliferation and immune cell infiltration. Limonene, the major component of orange peel essential oil, has also demonstrated anti-inflammatory activity in various models [17].

Antioxidant Activity: Psoriasis is associated with increased oxidative stress, which contributes to

inflammation and tissue damage. The rich array of flavonoids, phenolic acids, and carotenoids in *Citrus sinensis* peel extract exhibits potent antioxidant properties, scavenging free radicals and reducing oxidative damage [18].

Hesperidin, in particular, has shown significant antioxidant activity, protecting cells from oxidative stress-induced damage [19].

Antiproliferative Activity: The hyperproliferation of keratinocytes is a hallmark of psoriasis. Some studies suggest that certain compounds in *Citrus sinensis* peel extract may inhibit keratinocyte proliferation. For instance, flavonoids have been shown to modulate cell cycle progression and induce apoptosis in various cell types [20]. While direct evidence of the antiproliferative effects of orange peel extract on psoriatic keratinocytes is limited, its potential in this area warrants further investigation.

Modulation of Immune Response: Psoriasis is an immune-mediated disease, and modulating the aberrant immune response is crucial for its management. Flavonoids from citrus fruits have been shown to influence the activity of immune cells, such as T cells and dendritic cells, which are central to the pathogenesis of psoriasis [21]. Hesperidin has been reported to suppress T cell proliferation and cytokine production [22].

Skin Barrier Function: A compromised skin barrier is observed in psoriatic skin, contributing to increased permeability and inflammation. Some studies suggest that certain flavonoids can improve skin barrier function by promoting the synthesis of lipids and structural proteins in the epidermis [23].

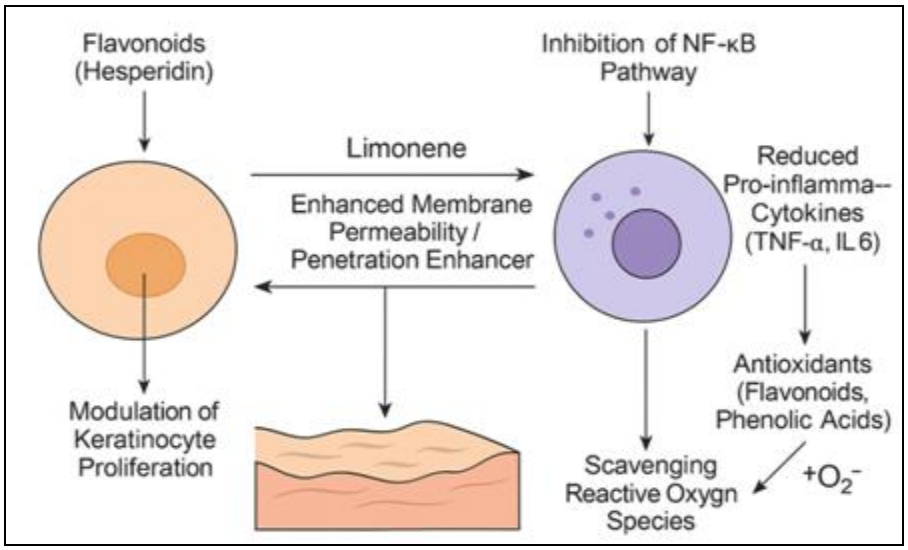

FIG. 1: POTENTIAL MECHANISMS OF ACTION OF *CITRUS SINENSIS* PEEL EXTRACT IN PSORIASIS

***Linum usitatissimum* (Flaxseed) Oil:**

Botanical Description and Traditional Uses: *Linum usitatissimum*, belonging to the family Linaceae, is an annual herb cultivated for its seeds and fibers. Flaxseed has been used for centuries for its nutritional and medicinal properties. The oil extracted from flaxseed is particularly rich in alpha-linolenic acid (ALA), an omega-3 polyunsaturated fatty acid [24]. In traditional medicine, flaxseed and flaxseed oil have been used for various ailments, including gastrointestinal disorders, coughs, and skin conditions. Topically, flaxseed oil has been used to soothe irritated skin, promote wound healing, and improve skin hydration [25].

Major Constituents: The primary constituents of *Linum usitatissimum* oil include:

Omega-3 Fatty Acids: Alpha-linolenic acid (ALA) constitutes approximately 50-60% of the fatty acids in flaxseed oil. ALA is an essential fatty acid that can be converted to other omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), in the body [26].

Omega-6 Fatty Acids: Linoleic acid (LA) is another significant polyunsaturated fatty acid present in flaxseed oil.

Omega-9 Fatty Acids: Oleic acid is a monounsaturated fatty acid also found in flaxseed oil.

Other Compounds: Flaxseed oil also contains minor amounts of saturated fatty acids, vitamins (e.g., vitamin E), and lignans (though lignans are more abundant in the flaxseed meal than the oil) [27].

Pharmacological Properties Relevant to Psoriasis: The high content of omega-3 fatty acids in *Linum usitatissimum* oil contributes to several pharmacological properties relevant to the management of psoriasis:

Anti-inflammatory Activity: Omega-3 fatty acids, particularly EPA and DHA derived from ALA metabolism, have potent anti-inflammatory effects. They can reduce the production of pro-inflammatory eicosanoids (e.g., prostaglandins and leukotrienes) derived from arachidonic acid (an omega-6 fatty acid) and promote the synthesis of anti-inflammatory mediators [28]. In psoriasis, reducing inflammation is a key therapeutic goal.

Modulation of Immune Response: Omega-3 fatty acids can influence the function of immune cells, including T cells and neutrophils, which are implicated in the pathogenesis of psoriasis. They have been shown to suppress the production of pro-inflammatory cytokines and chemokines, thereby modulating the immune response in psoriasis [29].

Improvement of Skin Barrier Function: Essential fatty acids, including omega-3 and omega-6, are crucial components of the epidermal lipid barrier.

Topical application of flaxseed oil, rich in these fatty acids, can help to restore and maintain the integrity of the skin barrier in psoriatic skin, reducing transepidermal water loss and improving hydration [30] A compromised skin barrier exacerbates inflammation in psoriasis.

Antipruritic Effect: Pruritus (itching) is a common and distressing symptom of psoriasis. Some studies suggest that omega-3 fatty acids can have an antipruritic effect by modulating inflammatory pathways and nerve endings in the skin [31]. Topical application of flaxseed oil may help to alleviate itching associated with psoriatic lesions.

Reduction of Scaling: The characteristic scaling in psoriasis is due to hyperproliferation of keratinocytes and abnormal differentiation. While direct evidence of flaxseed oil's effect on keratinocyte proliferation is limited, its anti-inflammatory and skin barrier-improving properties may indirectly contribute to a reduction in scaling by normalizing epidermal turnover and improving hydration [32].

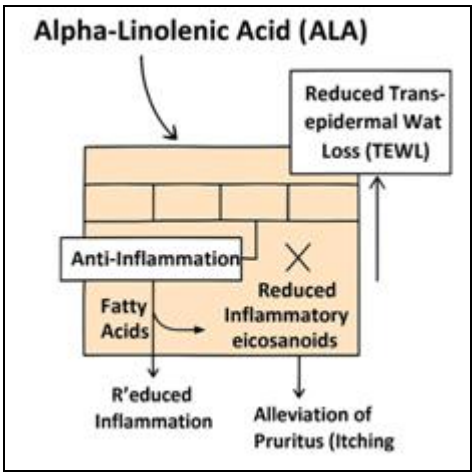

FIG. 2: POTENTIAL MECHANISMS OF ACTION OF *LINUM USITATISSIMUM* OIL IN PSORIASIS

Rationale for Combining *Citrus sinensis* Peel Extract and *Linum usitatissimum* Oil in a Polyherbal Cream: The combination of *Citrus sinensis* peel extract and *Linum usitatissimum* oil in a polyherbal cream offers a synergistic approach to address the multifaceted pathology of psoriasis [33]:

Complementary Anti-inflammatory Mechanisms: Both ingredients exhibit significant anti-inflammatory properties through different mechanisms. *Citrus sinensis* peel extract, rich in flavonoids and limonene, can inhibit pro-inflammatory cytokine production. *Linum usitatissimum* oil, with its high omega-3 content, can modulate eicosanoid pathways and also influence cytokine production. Combining these may lead to a more potent and broader anti-inflammatory effect.

Combined Antioxidant Activity: Psoriasis is associated with increased oxidative stress. The antioxidant properties of flavonoids, phenolic acids, and carotenoids in orange peel extract, combined with the potential antioxidant effects of vitamin E and other minor components in flaxseed

oil, can provide enhanced protection against oxidative damage in psoriatic skin.

Addressing Keratinocyte Hyperproliferation and Differentiation: While direct antiproliferative effects of both ingredients on psoriatic keratinocytes need further investigation, the reduction in inflammation achieved by their combination may indirectly help to normalize keratinocyte proliferation and differentiation. Additionally, some flavonoids have shown potential in modulating these processes.

Improving Skin Barrier Function and Hydration: *Linum usitatissimum* oil is rich in essential fatty acids that are crucial for maintaining the integrity of the epidermal lipid barrier and reducing transepidermal water loss. While *Citrus sinensis* peel extract's direct impact on skin barrier function is less established, its anti-inflammatory effects can indirectly support barrier repair by reducing inflammation-induced damage. Improved skin hydration can also alleviate scaling and discomfort associated with psoriasis.

Potential for Enhanced Efficacy and Reduced Side Effects: By combining ingredients with complementary mechanisms of action, it may be possible to achieve better therapeutic outcomes at lower concentrations of individual components, potentially reducing the risk of side effects associated with high concentrations of a single active agent.

Traditional Use and Safety Profile: Both *Citrus sinensis* peel and flaxseed oil have a history of traditional use for skin conditions and are generally considered safe for topical application when used appropriately.

TABLE 1: SUMMARY OF THE BIOACTIVE COMPOUNDS AND THEIR PHARMACOLOGICAL ACTIVITIES

Ingredient	Key Bioactive Compounds	Relevant Pharmacological Activities
Citrus sinensis Peel Extract	Hesperidin, Limonene, other Flavonoids, Phenolic Acids, Carotenoids	Anti-inflammatory (cytokine inhibition), Antioxidant, Potential antiproliferative, Immunomodulatory, Potential improvement of skin barrier function
Linum usitatissimum Oil	Alpha-linolenic acid (ALA), Linoleic acid, Oleic acid	Anti-inflammatory (eicosanoid modulation, cytokine inhibition), Immunomodulatory, Improvement of skin barrier function, Antipruritic, Potential reduction of scaling

Formulation Aspects of a Polyherbal Cream: Developing an effective polyherbal cream requires careful consideration of several formulation aspects to ensure optimal delivery of the active compounds to the target site in the skin and maintain product stability and patient compliance [34].

Extraction Methods: The method used to extract bioactive compounds from *Citrus sinensis* peel can significantly affect the yield and composition of the extract. Techniques such as solvent extraction (e.g., using ethanol, methanol, or hydroalcoholic mixtures), supercritical fluid extraction, and microwave-assisted extraction can be employed. The choice of solvent and extraction conditions should be optimized to maximize the extraction of desired flavonoids, phenolic acids, and essential oils while minimizing the extraction of unwanted compounds.

Oil Quality and Processing: The quality of *Linum usitatissimum* oil is crucial. Cold-pressed oil is preferred as it retains a higher content of bioactive compounds and is less prone to oxidation. The oil should be properly stored to prevent rancidity.

Cream Base Selection: The choice of cream base (e.g., oil-in-water or water-in-oil emulsion) will influence the release and penetration of the active ingredients. Oil-in-water creams are generally preferred for topical applications as they are non-greasy and easily washable. The cream base should be compatible with both the aqueous extract of *Citrus sinensis* peel (if used) and the oil of *Linum usitatissimum*.

Concentration of Active Ingredients: The optimal concentrations of *Citrus sinensis* peel extract and *Linum usitatissimum* oil in the cream need to be determined based on their individual efficacy, potential for irritation, and synergistic effects. Dose-response studies may be required to identify the most effective and safe concentrations.

Penetration Enhancers: The stratum corneum, the outermost layer of the skin, acts as a barrier to the

penetration of many topical agents. The inclusion of penetration enhancers, such as oleic acid, propylene glycol, or terpenes (some of which may be present in the essential oil component of orange peel extract), may be necessary to improve the delivery of the active compounds to the deeper layers of the epidermis and dermis where the pathological processes of psoriasis occur.

Stabilizing Agents and Preservatives: Polyherbal formulations can be complex and may be more susceptible to microbial contamination and degradation. The inclusion of appropriate preservatives (e.g., parabens, phenoxyethanol) and stabilizing agents (e.g., antioxidants, emulsifiers) is essential to ensure product safety and stability over its shelf life.

pH and Viscosity: The pH of the cream should be compatible with the skin's natural pH (around 4.5-5.5) to avoid irritation. The viscosity should be appropriate for easy application and spreadability.

Compatibility Studies: It is crucial to conduct compatibility studies to ensure that the components of the *Citrus sinensis* peel extract and *Linum usitatissimum* oil are compatible with each other and with the cream base, and that there are no adverse interactions that could affect the stability or efficacy of the product [35].

Epidemiology and Demographics: The global prevalence of psoriasis, while substantial, shows variations across geographical regions and ethnic groups, with higher rates observed in Caucasian populations and lower rates in East Asians and Africans. The disease exhibits a bimodal age of onset: an early onset form, typically manifesting in young adulthood (15-30 years), often associated with a stronger genetic predisposition and more severe disease, and a later onset form (50-60 years), which may have weaker genetic links.

A strong genetic component is undeniable, with approximately one-third of individuals reporting a family history of psoriasis. The PSORS1 locus on chromosome 6, containing the *HLA-Cw6* allele, is the strongest genetic risk factor, particularly for early-onset and guttate forms. However, psoriasis is a polygenic disease, with numerous other susceptibility genes identified, many of which are involved in immune regulation.

Beyond genetics, environmental triggers are crucial for disease initiation and exacerbation in genetically predisposed individuals [6].

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Infections: Streptococcal infections (especially *Streptococcus pyogenes*) are classic triggers for guttate psoriasis, particularly in children and adolescents. HIV infection can also significantly alter the course and severity of psoriasis.

Stress: Psychological stress is a well-recognized precipitating factor for psoriasis flares, highlighting the intricate brain-skin axis.

Trauma (Koebner Phenomenon): Psoriatic lesions can emerge at sites of skin injury, such as scratches, surgical incisions, or sunburns, demonstrating the skin's heightened inflammatory response.

Medications: Certain drugs can induce or worsen psoriasis. These include:

Beta-blockers: Commonly used for hypertension and cardiac conditions.

Lithium: A mood stabilizer used in psychiatric disorders.

Antimalarials: Such as chloroquine and hydroxychloroquine.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs): Can sometimes exacerbate existing psoriasis.

Corticosteroid withdrawal: Abrupt cessation of systemic corticosteroids can trigger severe rebound flares, including generalized pustular psoriasis.

Lifestyle Factors: Smoking is consistently linked to increased psoriasis severity and incidence. Excessive alcohol consumption can also exacerbate the disease and interfere with treatment. Obesity is another significant factor, correlating with increased disease severity and reduced response to therapies.

Pathophysiology:

The Immune Dysregulation Cascade: The hallmark of psoriasis is an accelerated epidermal turnover, where keratinocytes mature and shed in a mere 3-5 days, drastically faster than the normal 28-30 days. This hyperproliferation is not intrinsic to keratinocytes but is a downstream effect of a complex and sustained immune dysregulation. The current understanding centers on a pathological immune cascade driven primarily by T-helper 17 (Th17) and T-helper 1 (Th1) cell pathways [34]. The intricate interplay begins with various triggers (genetic, environmental, microbial) that activate dendritic cells (DCs) in the skin. These antigen-presenting cells are crucial orchestrators of the immune response:

Activation of DCs: Upon activation, DCs mature and migrate to regional lymph nodes, where they present antigens to naive T cells. Critically, activated DCs produce a plethora of pro-inflammatory cytokines, including Interleukin-12 (IL-12) and Interleukin-23 (IL-23) [17].

T-Cell Differentiation and Activation: IL-12 primarily drives the differentiation of naive CD4+ T cells into Th1 cells. These Th1 cells then migrate to the skin and release Interferon-gamma (IFN-γ) and Tumor Necrosis Factor-alpha (TNF-α). IFN-γ further activates keratinocytes and DCs, while TNF-α is a potent pro-inflammatory cytokine that promotes inflammation, angiogenesis, and keratinocyte proliferation. IL-23 is the master cytokine responsible for the differentiation, survival, and expansion of Th17 cells. These Th17 cells, once activated, migrate to the skin and produce a potent array of cytokines, including Interleukin-17A (IL-17A), Interleukin-17F (IL-17F), and Interleukin-22 (IL-22). IL-17A is particularly central to psoriatic pathology. It directly stimulates keratinocytes to proliferate and produce antimicrobial peptides (e.g., psoriasin, LL-37) and chemokines (e.g., CXCL1, CXCL8/IL-8) that recruit neutrophils and other inflammatory cells. This creates a self-perpetuating cycle of inflammation. IL-22 also contributes to keratinocyte hyperproliferation and epidermal thickening.

Keratinocyte Response: Keratinocytes are not merely passive targets; they actively participate in the inflammatory loop. In response to cytokines like IL-17, TNF-α, and IFN-γ, they proliferate excessively and release their own pro-inflammatory mediators, including chemokines (e.g., CCL20, CXCL10) that attract more immune cells, amplifying the inflammatory cascade.

Neutrophils: Recruited by chemokines (like IL-8), neutrophils infiltrate psoriatic lesions, forming microabscesses (Munro's microabscesses) within the epidermis, particularly prominent in pustular forms of psoriasis. They also release inflammatory mediators and reactive oxygen species [18]. The detailed understanding of these specific immune pathways and key cytokines has been pivotal in the development of highly targeted biologic therapies, allowing for precise intervention at different points in the inflammatory cascade [20].

Clinical Phenotypes and Variants: Psoriasis is a highly polymorphic disease, presenting with a wide array of clinical manifestations that can vary in morphology, distribution, and severity. Accurate classification is essential for guiding treatment [21].

Chronic Plaque Psoriasis (Psoriasis Vulgaris): This is the most common form, accounting for approximately 80-90% of cases. It is characterized by well-demarcated, erythematous (red) plaques covered with silvery-white, adherent scales.

These lesions typically appear symmetrically on extensor surfaces (e.g., elbows, knees), the scalp, sacral area, and lower back. Plaques can range from a few millimeters to several centimeters in size and may coalesce to form larger patches.

Patients often experience significant pruritus (itching) and discomfort, with painful fissures sometimes developing within thick plaques.

Guttate Psoriasis: Characterized by the sudden eruption of numerous small, droplet-like (guttate, from Latin *gutta* meaning drop) lesions over the trunk and proximal extremities. It often follows a streptococcal upper respiratory tractinfection (e.g., pharyngitis) by 2-3 weeks, especially in children and young adults. While it can resolve spontaneously, it may also evolve into chronic plaque psoriasis.

Inverse (Flexural) Psoriasis: Also known as intertriginous psoriasis, this variant occurs in skin folds, such as the armpits (axillae), groin, inframammary folds, and umbilical region.

The lesions are typically smooth, shiny, erythematous patches, often lacking the characteristic silvery scales due to moisture and friction in these areas. It is frequently misdiagnosed as fungal or bacterial infections, making proper diagnosis crucial.

Pustular Psoriasis: A more severe and less common form characterized by the presence of sterile pustules (blisters filled with white blood cells).

Localized Pustular Psoriasis (e.g., Palmoplantar Pustulosis - PPP): Affects the palms and soles, leading to recurrent crops of pustules, erythema, and scaling. It can be highly debilitating due to pain and difficulty with ambulation or manual tasks [22].

Generalized Pustular Psoriasis (GPP): A life-threatening medical emergency characterized by widespread erythema and crops of sterile pustules covering large areas of the body, often accompanied by fever, malaise, leukocytosis, and other systemic symptoms (e.g., arthralgia, elevated inflammatory markers, liver dysfunction). Triggers include systemic corticosteroid withdrawal, infections, and certain medications. Requires urgent hospitalization and systemic treatment.

Erythrodermic Psoriasis: This is another severe and potentially life-threatening variant where psoriasis affects more than 90% of the body surface. The skin becomes intensely red, swollen, and covered with fine scales, leading to generalized shedding.

The extensive skin inflammation disrupts the skin's barrier function, leading to significant thermoregulation abnormalities (hypothermia or hyperthermia), fluid and electrolyte imbalance (dehydration, edema), and increased risk of secondary infections and high-output cardiac failure. Patients are often acutely ill and require hospitalization.

Nail Psoriasis: Affects up to 50% of individuals with cutaneous psoriasis and an astonishing 80% of those with psoriatic arthritis. Nail manifestations are diverse and can include:

Pitting: Small depressions on the nail surface.

Onycholysis: Separation of the nail plate from the nail bed.

Subungual Hyperkeratosis: Thickening and crumbling of the nail due to scale buildup under the nail plate.

Oil Spots/Salmon Patches: Translucent, yellowish-red discoloration under the nail plate.

Splinter Hemorrhages: Small, thin, reddish-brown lines under the nail. Nail psoriasis can cause pain, functional impairment, and significant cosmetic distress, and it is often resistant to topical treatments, frequently requiring systemic therapy.

Scalp Psoriasis: Extremely common and often one of the most bothersome forms, affecting up to 80% of psoriasis patients. It presents as thick, silvery scales on an erythematous base, often extending beyond the hairline. Severe itching and flaking can be distressing and lead to social embarrassment. Hair shafts typically grow through the scales, but severe cases can result in temporary hair loss. Treatment is challenging due to the hair impeding topical application.

The Burden of Disease and Comorbidities: The impact of psoriasis extends far beyond its visible skin manifestations, imposing a substantial

physical, psychological, social, and economic burden on affected individuals and healthcare systems. Moreover, its systemic inflammatory nature significantly increases the risk of various comorbidities, underscoring the need for a holistic management approach.

Physical Burden: Patients experience chronic symptoms like intense pruritus, which can lead to sleep disturbances, excoriations, and secondary infections.

Painful skin cracking (fissures), particularly on palms and soles, and bleeding from lesions, can severely impair daily activities, occupational performance, and overall physical comfort. The physical discomfort significantly reduces quality of life (QoL).

Psychological Burden: Psoriasis carries a heavy psychological toll, driven by the highly visible nature of the disease and societal misconceptions. Patients frequently report feelings of embarrassment, shame, self-consciousness, and stigmatization. This can lead to social isolation, avoidance of public activities (e.g., swimming), and difficulties in relationships. The chronic nature and unpredictable flares contribute to high rates of depression, anxiety, and in severe cases, even suicidal ideation. Healthcare providers must actively screen for and address these mental health challenges.

Social and Economic Burden: The visible lesions and associated symptoms can lead to discrimination in social settings and at the workplace. Patients may face challenges in certain professions or experience reduced productivity due to discomfort and frequent medical appointments. The economic burden is substantial, encompassing direct medical costs (doctor visits, medications, phototherapy) and indirect costs (lost wages, reduced productivity).

Associated Comorbidities: The Systemic Link: The chronic systemic inflammation inherent in psoriasis is now recognized as a driver for numerous associated conditions, emphasizing that psoriasis is a systemic disease.

Psoriatic Arthritis (PsA): Affecting up to 30% of psoriasis patients, PsA is a chronic inflammatory arthritis that can lead to progressive and irreversible joint damage if untreated. It can manifest in various ways, including peripheral arthritis (often asymmetric oligoarthritis), axial involvement (spondylitis, sacroiliitis), enthesitis (inflammation at tendon/ligament insertion sites), and dactylitis ("sausage digits"). Early diagnosis and prompt treatment are critical to preserve joint function and prevent disability.

Cardiovascular Disease (CVD): Psoriasis patients have an independently increased risk of major adverse cardiovascular events (e.g., myocardial infarction, stroke, cardiovascular death), even after adjusting for traditional CVD risk factors like smoking, obesity, and diabetes. This heightened risk is attributed to the systemic inflammation causing endothelial dysfunction, accelerated atherosclerosis, and dyslipidemia.

Metabolic Syndrome: There is a significantly increased prevalence of metabolic syndrome in psoriasis patients, characterized by a cluster of conditions including obesity, type 2 diabetes mellitus, hypertension, and dyslipidemia. This bidirectional relationship means psoriasis patients are more prone to metabolic syndrome, and metabolic syndrome can worsen psoriasis severity.

Inflammatory Bowel Disease (IBD): Psoriasis shares common genetic susceptibility loci and inflammatory pathways (e.g., IL-23/IL-17 axis) with IBD (Crohn's disease and ulcerative colitis). Patients with psoriasis have an increased risk of developing IBD, and vice versa.

Mental Health Disorders: As previously noted, depression and anxiety are highly prevalent. The chronic nature of the disease, its visible manifestations, and the associated stigma contribute to psychological distress. It is essential to screen for these conditions and provide appropriate support, including psychological counseling or pharmacotherapy.

Other Comorbidities: Psoriasis has also been linked to other conditions such as non-alcoholic fatty liver disease (NAFLD), chronic kidney disease, uveitis, and obstructive sleep apnea.

Holistic Management and Special Considerations: Effective psoriasis management extends beyond mere pharmacological intervention.

It demands a holistic and patient-centered approach that addresses the physical, psychological, social, and comorbid aspects of the disease. This integrated strategy aims to optimize outcomes and enhance overall quality of life.

Lifestyle Modifications: Lifestyle factors play a crucial role in both the onset and exacerbation of psoriasis, and their modification can significantly impact disease severity and treatment response.

Weight Management: Obesity is strongly linked to increased psoriasis severity and often correlates with a poorer response to systemic therapies, particularly biologics. Adipose tissue is metabolically active, producing pro-inflammatory adipokines (e.g., leptin, TNF-α, IL-6) that contribute to systemic inflammation. Weight loss, even modest amounts, can lead to significant improvements in psoriasis severity and enhance the effectiveness of treatments.

Diet: While no single "psoriasis diet" is universally recommended, an anti-inflammatory dietary pattern is often beneficial. The Mediterranean diet, rich in fruits, vegetables, whole grains, lean proteins (fish, poultry), healthy fats (olive oil, nuts), and low in red meat and processed foods, has shown promise in reducing systemic inflammation.

Limiting excessive sugar intake, refined carbohydrates, and saturated fats is generally advised. Some patients report triggers from specific foods (e.g., gluten, dairy), but individualized dietary approaches should be discussed with a healthcare professional to ensure nutritional adequacy.

Smoking Cessation: Smoking is a well-established and significant risk factor for both the development of psoriasis and increased disease severity. It is also associated with reduced response to various psoriasis treatments. Encouraging and supporting smoking cessation is a critical intervention for all psoriasis patients.

Alcohol Moderation/Cessation: Excessive alcohol consumption can worsen psoriasis flares and may interact adversely with certain systemic medications like methotrexate, increasing the risk of hepatotoxicity. Patients should be advised on safe alcohol limits or encouraged to abstain.

Stress Management: Psychological stress is a powerful and well-documented trigger for psoriasis flares. Chronic stress can alter immune function and exacerbate inflammation. Incorporating stress-reduction techniques such as mindfulness, meditation, yoga, deep breathing exercises, and adequate sleep can significantly help mitigate disease activity and improve overall well-being.

Regular Exercise: Engaging in regular physical activity not only contributes to weight management but also reduces systemic inflammation, improves cardiovascular health, and boosts mood. Patients should be encouraged to find forms of exercise that are comfortable and enjoyable, adapting to any joint limitations if psoriatic arthritis is present.

Sunlight Exposure: Controlled, judicious exposure to natural sunlight can improve psoriasis due to its UVB component. However, caution against sunburn is paramount, as sunburn can trigger the Koebner phenomenon and increase skin cancer risk.

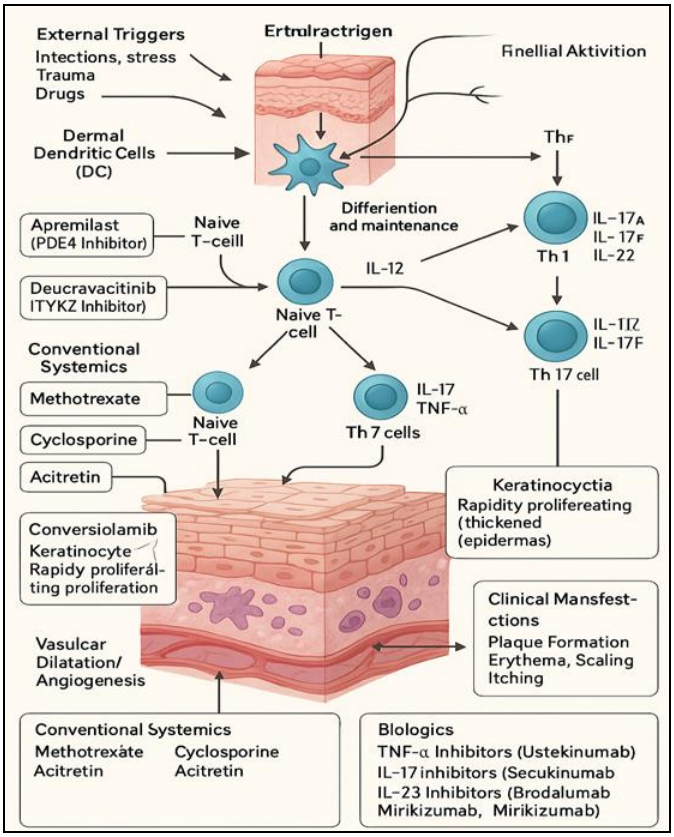

FIG. 3: MANAGEMENT OF PSORIASIS

The Therapeutic Power of Key Herbal Components: The selection of *Citrus sinensis* and *Linum usitatissimum* for a psoriatic cream is based

on their distinct yet complementary Pharmacological profiles, which directly address the primary symptoms and underlying mechanisms of the disease [6].

***Citrus sinensis* (Sweet Orange) Oil: Phytochemicals and Anti-Psoriatic Potential:** *Citrus sinensis* (L.) Osbeck, commonly known as sweet orange, is a globally cultivated fruit of the Rutaceae family. While the pulp and juice are consumed worldwide, the peel, which constitutes a significant portion of the fruit's weight, is often discarded as a processing by product. However, the peel is a veritable reservoir of bioactive compounds with a wide range of pharmacological properties, making it an invaluable resource for medicinal applications.

Botanical Profile and Ethnomedicinal Relevance: In traditional medicine systems, different parts of the *Citrus* species have been used for centuries. In traditional Chinese medicine, the dried peel of *Citrus reticulata* (*chenpi*) is a well-known herbal remedy for digestive issues and respiratory ailments. Similarly, in Ayurvedic and Unani medicine, citrus peels have been employed for their carminative, antiseptic, and anti-inflammatory effects. Topically, preparations from orange peel have been traditionally used to promote wound healing, brighten skin, and soothe minor skin irritations. This rich history of use provides a strong foundational basis for investigating its modern dermatological applications, particularly for chronic inflammatory conditions like psoriasis [10].

A Deep Dive into Key Bioactive Constituents and Their Mechanisms: The therapeutic efficacy of *C. sinensis* peel extract is primarily attributed to three major classes of compounds: flavonoids, essential oils, and phenolic acids.

Flavonoids: The most prominent flavonoid in sweet orange peel is hesperidin, a glycoside that is metabolized into its aglycone, hesperetin. Hesperidin is a potent anti-inflammatory and antioxidant agent [53]. At the cellular level, hesperidin exerts its anti-inflammatory effects by inhibiting the activation of the NF-κBsignaling pathway. NF-κB is a master transcription factor that, when activated, upregulates the expression of numerous pro-inflammatory genes, including those for cytokines like TNF-α, IL-6, and IL-8. These cytokines are central to the inflammatory cascade in psoriasis, driving both the infiltration of immune cells and the hyperproliferation of keratinocytes. By blocking NF-κB, hesperidin can effectively dampen this inflammatory response. Furthermore, *in-vitro* studies have shown that hesperidin possesses antiproliferative effects on various cell lines, suggesting its potential to directly modulate the rapid cell turnover that is a hallmark of psoriatic skin. Other flavonoids, such as naringin and tangeretin, also contribute to these effects.

Essential Oils (Limonene): The essential oil of sweet orange peel is overwhelmingly composed of limonene (typically >90%). This monoterpene contributes to the fruit's characteristic aroma and possesses a wide array of biological activities. Limonene has demonstrated significant anti-inflammatory and antioxidant properties in various preclinical models. Crucially, its lipophilic nature makes it an effective skin penetration enhancer. The stratum corneum, the outermost layer of the epidermis, acts as a formidable barrier to the absorption of many topical agents. By disrupting the ordered lipid structure of the stratum corneum, limonene can improve the percutaneous absorption of other active compounds in a cream, ensuring that flavonoids and other therapeutic molecules can reach the deeper epidermal and dermal layers where the pathological processes of psoriasis are taking place.

Antioxidants: The combination of flavonoids, phenolic acids (e.g., ferulic acid), and carotenoids in orange peel provides a robust antioxidant defense system. Psoriasis is known to be associated with increased oxidative stress, which contributes to chronic inflammation and cellular damage. The potent antioxidant activity of the peel extract helps to neutralize reactive oxygen species (ROS), thereby mitigating the oxidative damage that exacerbates the disease.

***Linum usitatissimum* (Flaxseed) Oil: Omega-3s for Skin Health:** *Linum usitatissimum*, commonly known as flax, is an annual herb cultivated globally for its seeds and fibers. Flaxseed oil, extracted by pressing the seeds, has a unique and highly beneficial fatty acid profile that is particularly well-suited for dermatological applications.

Botanical Profile and Ethnomedicinal Use: Flax has a rich history as one of the oldest cultivated crops, with evidence of its use dating back to ancient civilizations. Historically, flaxseed and its oil have been used as a food source and in traditional medicine for a variety of ailments. Topically, flaxseed oil has been traditionally employed for its emollient and soothing properties, used to treat dry, irritated skin, and to promote wound healing. This traditional knowledge highlights its long-standing recognition as a valuable agent for skin health.

Omega-3 Fatty Acids and Their Anti-Psoriatic Role: The primary therapeutic component of flaxseed oil is its remarkably high concentration of alpha-linolenic acid (ALA), an omega-3 polyunsaturated fatty acid (PUFA), which typically constitutes 50-60% of the oil's fatty acid content. ALA is an essential fatty acid, meaning it cannot be synthesized by the human body and must be obtained from dietary or topical sources.

Modulation of the Eicosanoid Pathway: This is a core mechanism of action for ALA. In the body, ALA can be metabolized into longer-chain omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These omega-3s compete with arachidonic acid (an omega-6 fatty acid, which is abundant in the Western diet) for the same enzymes (cyclooxygenase and lipoxygenase). This competition leads to a shift in the production of eicosanoids. While arachidonic acid generates highly pro-inflammatory eicosanoids (e.g., prostaglandin textE_2 and leukotriene textB_4), the omega-3s lead to the production of less inflammatory eicosanoids (e.g., prostaglandin textE_3 and leukotriene textB_5). By modulating this balance, flaxseed oil can effectively dampen the chronic inflammatory response that drives psoriasis.

Skin Barrier Integrity: Essential fatty acids are crucial building blocks for the epidermal lipid matrix, which forms the skin's primary barrier. This barrier is composed of ceramides, cholesterol, and free fatty acids, and its integrity is often compromised in psoriatic skin, leading to increased transepidermal water loss (TEWL) and dryness. Topical application of flaxseed oil provides a direct supply of ALA, which is essential for the synthesis of these structural lipids. By helping to restore the integrity of the skin barrier, flaxseed oil improves skin hydration, reduces scaling, and protects against external irritants that can trigger psoriatic flares.

Symptomatic Relief: Beyond its fundamental anti-inflammatory and barrier-repairing effects, flaxseed oil directly addresses some of the most bothersome symptoms of psoriasis. By reducing inflammation and improving skin hydration, it can significantly alleviate pruritus (itching), which is a common and distressing symptom, and reduce the characteristic redness and scaling of psoriatic plaques.

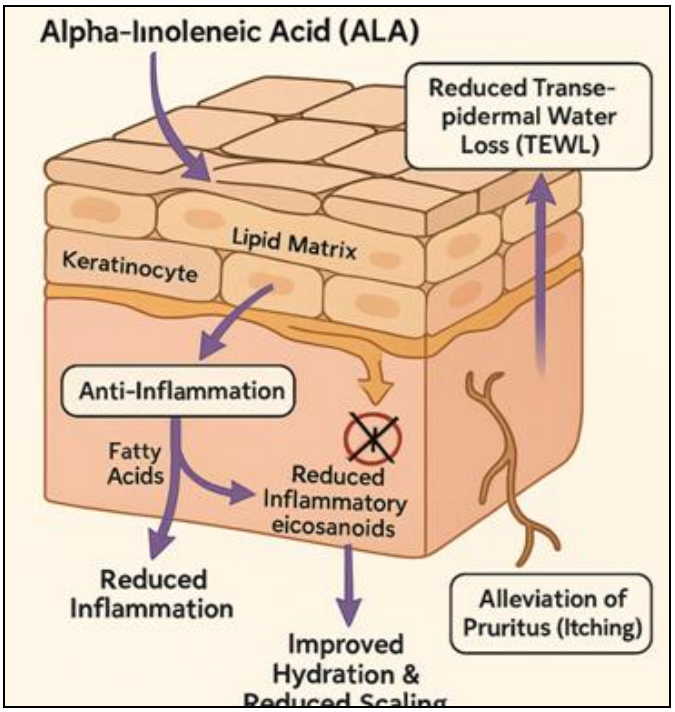

FIG. 4: POTENTIAL MECHANISMS OF ACTION OF *LINUM USITATISSIMUM* OIL IN PSORIASIS

The Synergistic Potential of the Polyherbal Formulation: The true therapeutic strength of this polyherbal cream lies in the synergy between its two primary components. This combination provides a multifaceted attack on the pathogenesis of psoriasis [16].

TABLE 2:

Feature	*Citrus sinensis* Oil	*Linum usitatissimum* Oil	Combined Synergistic Effect
Anti-Inflammation	Directly inhibits NF-κB, suppressing pro-	Provides anti-inflammatory ALA, which modulates	**A dual-action anti-inflammatory strategy** that targets two distinct but interconnected pathways,

	inflammatory cytokines like TNF-α.	eicosanoid metabolism.	leading to a more profound reduction in inflammation.
Antioxidant Action	d-limonene and flavonoids scavenge free radicals, reducing oxidative stress.	Lignans and fatty acids provide antioxidant protection.	A comprehensive antioxidant defense that protects skin cells from the damaging effects of ROS, which are exacerbated in psoriatic skin.
Skin Barrier	Acts as a permeation enhancer, aiding in the delivery of other actives.	Provides essential fatty acids that are critical for restoring the lipid barrier.	The permeation-enhancing effect of d-limonene ensures that the barrier-repairing fatty acids from flaxseed oil are delivered effectively to the target sites within the epidermis.

Formulation Considerations and Quality Control: The development of a stable and effective polyherbal cream is a complex process that demands meticulous attention to detail.

Emulsion Stability: Creating a stable cream requires a precise balance of oil-phase and water-phase components, along with a suitable emulsifying system. The incorporation of essential oils and fatty acids can be challenging due to their different polarities, necessitating the use of co-emulsifiers and stabilizers to prevent phase separation.

Optimal Concentrations: The concentration of each active oil must be carefully optimized. Too high a concentration of *C. sinensis* oil could lead to skin irritation or sensitization (especially in the presence of UV light), while an insufficient amount would render it therapeutically ineffective. Similarly, the percentage of flaxseed oil needs to be adequate to provide significant barrier-repairing effects without making the cream excessively greasy.

Preservation and Stability: Due to its natural origins, the cream is susceptible to microbial contamination and oxidative degradation. The high concentration of unsaturated fatty acids in flaxseed oil makes it particularly vulnerable to oxidation. Therefore, the formulation must include effective preservatives and antioxidants (e.g., Vitamin E) to ensure a long shelf life and product safety [22].

Standardization and Quality Assurance: To guarantee the consistency of the final product, the raw herbal oils must be standardized. This involves using analytical techniques (e.g., Gas Chromatography-Mass Spectrometry) to quantify key biomarkers like d-limonene and ALA in every batch. This ensures that each tube of cream delivers a consistent and predictable dose of active compounds [25].

CONCLUSION: The development of a polyherbal cream combining the therapeutic properties of *Citrus sinensis* peel extract and *Linum usitatissimum* oil represents a significant and scientifically sound approach to managing psoriasis. The individual and synergistic effects of these two natural ingredients target the core pathological features of the disease inflammation, oxidative stress, and epidermal dysfunction. By combining a potent anti-inflammatory flavonoid source with a crucial skin barrier-repairing omega-3 oil, this formulation has the potential to offer a safe, effective, and affordable alternative or complementary treatment for millions of psoriasis sufferers. The local availability of these plants in many regions, including Aligarh, Uttar Pradesh, India, makes this an especially compelling prospect. Continued research, including rigorous preclinical and clinical studies, is essential to validate this innovative therapeutic strategy and bring a promising new option to the dermatology toolkit, bridging the gap between traditional wisdom and modern science to create accessible and effective healthcare solutions.

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