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Review Article

Exploring the Potential of Thymoquinone and Hydrocortisone Cream for Inflammatory Skin Conditions: A Review Article

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Abstract

The review study investigates the possibility of using hydrocortisone and thymoquinone together as a medical cream to treat inflammatory skin diseases such as acne, eczema, and psoriasis. The well-known anti-inflammatory actions of hydrocortisone are enhanced by the anti-inflammatory, antioxidant, and wound-healing qualities of thymoquinone, which is derived from Nigella sativa seeds. There is a noticeable lack of prescription creams with these substances, indicating a market gap, even though skin problems are chronic and there are treatment alternatives available. The review highlights the advantages of creams as the recommended dose form because of their ease of use, quick absorption, and patient choice. It also mentions the growing popularity of herbal and natural skincare products, which is consistent with thymoquinone's potential. In order to meet the unmet requirements of patients with dermatological conditions and progress pharmacotherapy in this area, the study recommends the creation and evaluation of a thymoquinone and hydrocortisone cream.

Keywords

Anti-inflammatory Properties, Topical Drug Delivery System, Health Related Quality of Life, Chronic Inflammatory Skin Disease

1. Introduction

Pharmaceutical creams are semi-solid formulations consisting of one or more therapeutic ingredients dissolved or disseminated in an o/w emulsion, water washable basis, or water in oil (w/o) [1]. This review focuses on importance of thymoquinone and hydrocortisone cream because thymoquinone has an anti-inflammatory, anti-oxidant, wound healing and may have tumor reducing properties, as it can be beneficial for skin conditions like psoriasis, eczema and acne. [2] As about black seeds (*Nigellia sativa*) Prophet Muhammad (Peace be upon Him) stated that shooneez is a cure of all ailments expect death. [3]

1.1. Topical Drug Delivery System

Over the course of the last several decades, many methods of drug administration, including oral, sublingual, rectal, parental, topical, and inhalation have been used to treat illnesses in humans. When a drug-containing formulation is

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applied topically to treat a cutaneous condition or the skin-related symptoms of a general illness (like psoriasis), this is referred to as "topical delivery". The intention is to limit the pharmacological effects of the medicine to the skin's surface or inside its layers. The majority of topical administration methods employ semisolid formulations, while foams, solutions, sprays, medicated powders, and even medicated adhesive drug delivery systems are also in use. [4]

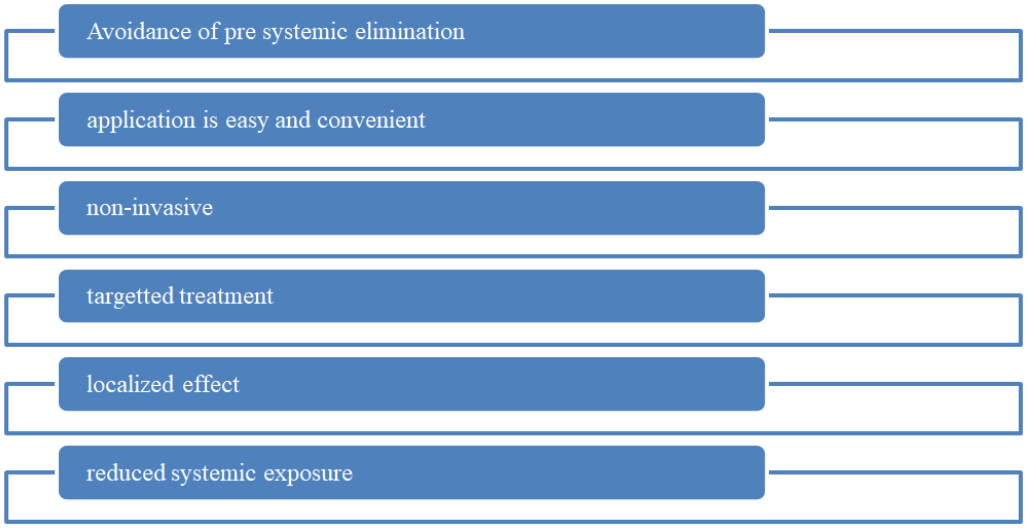

Figure 1. *Advantages of topical drug delivery system.*

1.2. Physiology of Human Skin

The largest organ in the body is the skin, which is around fifteen percent of total body weight of adult. It regulates a wide range of vital functions, including protecting the body from external physical, chemical, and biological hazards, limiting excessive water loss, and assisting with thermoregulation. [5] The body's primary defensive mechanism against toxins and viruses is the skin. Its three main layers are the hypodermis, dermis, and stratum corneum. [6]

1.2.1. Epidermis

It lacks blood vessels. The thickness of it changes with location. For instance, the eyelids have the thinnest layer and the heels the thickest. Thick layers of skin can accumulate in areas of the body that are subjected to higher friction or weight bearing (e.g. where a pencil scrapes against your writing finger or a shoe grinds on your foot). Although it lacks nerves; the mid layers of the epidermis do contain free nerve terminals from the dermis. 5 layers make up the epidermis. [7]

Table 1. *Layers of epidermis and their features.*

Layers of epidermis	Characteristics	Reference
Stratum corneum	Made up of 15–30 layers of corneocytes, also known as squames, which are keratinocytes. These keratinocytes are deceased. They have a high keratin content, which gives the skin, hair, and nails an impermeable layer. The body is constantly losing this layer. The process of skin cell migration from the stratum basale replaces shed cells. The length of this procedure varies depending on age and certain medical issues, but it usually takes 30 days.	[8]
Stratum lucidum	Is made up of two or three layers of inactive keratinocytes. It is possible to shave it off or puncture it unknowingly. Only thick skin regions, such as the palms of hands and the soles of feet, exhibit it. Found in calluses.	
Stratum granulosum	The largest concentration of free nerve terminals extending from the dermis is found in this layer. Unencapsulated dendrites that emerge from a sensory neuron are known as free nerve ends. They are the most prevalent nerve endings in the skin and send sensory data regarding temperature changes, gentle contact, and painful stimuli. They are less susceptible, nevertheless, to sudden variations in stimulus.	[9]

Layers of epidermis	Characteristics	Reference
Stratum spinosum	Includes lymphocytes and Langerhans cells, which are crucial components of the immune system.	
Stratum basale	The sole layer that continuously divides to create new cells. In the stratum basale, keratinocytes are continuously created and ascend through the layers to the outermost layer. In the skin, keratinocytes are the predominant cell type. Because they are structural cells and carry out vital immunological tasks, they are essential to wound healing. Additionally, melanocytes are generated in the basale layer. Melanin, which they generate, is a factor in skin tone. There are roughly equal numbers of melanocytes in humans. Thus, the quantity of melanin that these melanocytes create in reaction to their surroundings determines the color of skin. Merkel cells, which are capable of combining neuronal and endocrine functions, are also present in this layer. Hormones and neurotransmitters generated locally can be synthesized and stored by them. They convey nociceptive signals and operate as mechanoreceptors for light and selective tactile perception, but not for harsh touch or vibration.	[10]

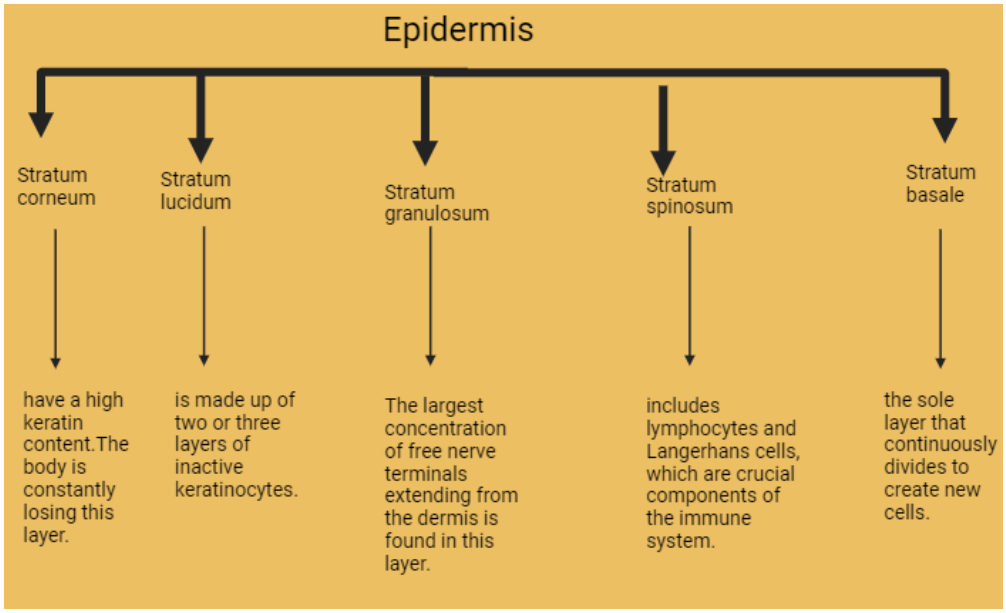

Figure 2. *General characteristics of epidermis.*

1.2.2. The Dermis

The dermis is strong and elastic. It is composed of connective tissue, with collagen fibers and elastic fibers woven together to form the matrix. Stretch marks, also known as persistent striae, are a result of the rupture of elastic fibers in the skin, which can happen during pregnancy or after obesity. Wrinkles appear as a result of the aging process because collagen fibers lose their capacity to bind water and provide the skin its tensile strength. The primary cells in the dermis are mast cells, fibroblasts, and macrophages. Varying levels of adipose (fat) tissue and areolar tissue lie under its lowest layer. [11] It has 2 layers which are as follows:

Table 2. *Layers of dermis and their features.*

Layers of dermis	Characteristics	References
Papillary layer	Interconnects with the skin's surface. This layer's ridges are what create our own fingerprints. Have fibroblasts, which are in charge of producing proteins, elastin, and collagen. Skin gains strength and	[12]

Layers of dermis	Characteristics	References
	flexibility from these properties. Have mast cells, which are crucial for the inflammatory response and the production of clots because they generate the chemicals histamine and heparin. Includes macrophages, which are important for the defense system, wound healing, and defense against cancer, hair growth and salt balance. Phagocytosis, in which phagocyte, a kind of white blood cell, engulfs and digests foreign cells and eliminates dead cells, is how they are recognized for eliminating foreign invaders. Contains leukocytes, which are essential to the inflammatory reaction that occurs after a skin injury. Leukocytes are necessary for both proper wound healing and infection clearance.	
Reticular layer	Situated halfway between the hypodermis, or subcutaneous layer, and the papillary layer. Collagen, blood arteries, nerve endings, T-cells, hair follicles, and glands are its constituent parts. Stem cells found in follicles of hair generate keratinocytes, which eventually develop into hair. They provide epithelial cells for closure of wounds, which is an important part of their involvement in wound healing-lymphocytes are in charge of eliminating infections and cancerous cells. Itching, touch, pressure, vibration, pain, and warmth are all sensed by nerves in the dermis. Damage to or exposure of nerves can cause pain from injuries that penetrate into the dermis.	[13]

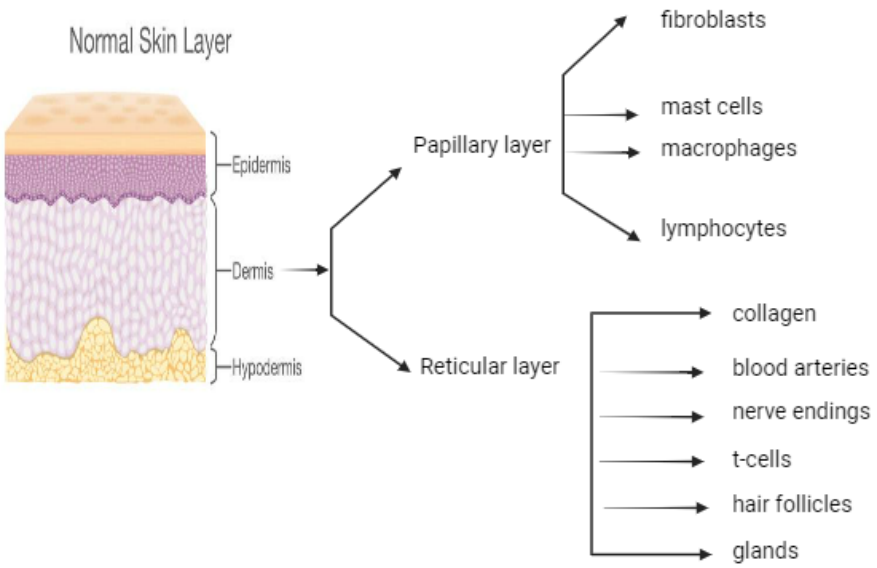

Figure 3. General characteristics of dermis.

1.2.3. Hypodermis

In the hypodermis, subcutaneous glands are located. Secretory epithelial cells, which originate from the same tissue as hair follicles, are the cells that comprise them. Except for the palms of hands and the soles of feet, they are present in every part of the body's skin. They release sebum, an oleaginous substance, into the hair follicles. The biggest concentration of them is found in the skin of the face, axillae, groin, and scalp. In areas like the lips, eyelids, nipple, labia minora, and glans penis where one kind of superficial epithelium changes into another, sebaceous glands that are not dependent on hair follicles release sebum directly onto the skin. [14]

1.3. Functions of Skin

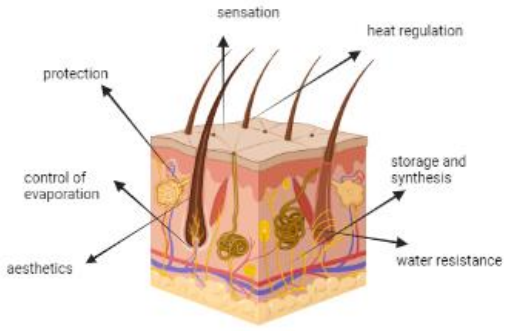

Figure 4. Functions of skin.

2. Pathogenesis of Inflammatory Skin Conditions

Skin conditions are known to significantly affect mental health, productivity, and enjoyment of life. [15].

2.1. Inflammatory Conditions

ROS, or reactive oxygen species, have advantages and disadvantages. Reactive oxygen species (ROS) are tightly regulated during normal physiological settings and are involved in cellular signaling as well as pathogen defense. On the other hand, excessive or inadequate ROS production results in oxidative stress, which damages cells. Numerous inflammatory illnesses have been connected to oxidative stress. In the initial phases of wound healing, inflammation serves as a vital defense against harmful assaults. However, inadequate resolution of inflammation may lead to a more severe, protracted reaction that damages more tissue. Inflammation-mediated tissue loss is the primary cause of many inflammatory skin disorders, including sunburn and psoriasis. Long-term overproduction of reactive oxygen species (ROS) present in the dermis may increase the risk of chronic inflammation or worsen damage caused by inflammation. Thus, a variety of pro- and antioxidants (enzymatic) are essential for preserving the cellular redox equilibrium. However, prolonged inflammation can decrease the antioxidant system, which might result in ongoing oxidative stress. [16]

2.2. Psoriasis

It is a chronic inflammatory skin disease that is autoimmune and has a strong genetic component. [17] It has a complicated pathophysiology, and the precise cause is yet unknown. [18] Major factors influencing the manifestation of the illness is early-onset of psoriasis (starting before age of forty) are the presence of the HLA-Cw6 (allele) and environmental triggers such β-haemolytic streptococcal infections. [19]

It is thought to be a mix of genetic, epigenetic, and environmental factors causes psoriasis. Exaggerated keratinocyte proliferation and altered differentiation, together with a significant infiltration of inflammatory cells, are characteristics of psoriatic skin lesions. Psoriatic skin is a result of the interaction of keratinocytes with T cells, inflammatory dendritic cells, and other cells. Specifically, dendritic cells that make interleukin 12 (IL-12) and IL-23 trigger T-helper-1 (Th1) and Th17 responses, which are essential for keratinocyte activation and the production of inflammatory molecules that amplify local defense mechanism, such as cytokines, chemokines, and antimicrobial peptides. [20]

An inflammatory immune-mediated disease with a strong genetic component is psoriasis. Given its association with psoriatic arthritis and the higher than average prevalence of cardiometabolic, hepatic, and mental comorbidities, therapy must be thorough and multidisciplinary. [21] Comorbidities with psoriasis can cause a major reduction in quality of life and huge expenses to society. [22] Individuals suffering from psoriasis are often linked to obesity, diabetes, dyslipidemia, cardiovascular disorders, and inflammatory bowel diseases (IBDs). [23]

2.3. Acne

Acne is an inflammatory skin disorder caused by sebaceous (oil) glands that link to hair follicles, which contain fine hair. Sebum is produced by the sebaceous glands and leaves the follicle through the pore in healthy skin. The follicle is lined with skin cells known as keratinocytes. Keratinocytes move toward the surface of the skin during normal skin cell shedding. When someone gets acne, sebum, keratinocytes, and hair all stick together inside the pore. In doing so, keratinocyte shedding and sebum penetration of the skin's surface are inhibited. Bacteria that normally live on the skin's surface may multiply in the blocked follicles due to the oil and cell combination, causing inflammation to manifest as redness, swelling, heat, and discomfort. The breakdown of the blocked follicle's wall allows sebum, skin cells, and bacteria to seep into the surrounding skin, resulting in lesions or pimples. [24]

2.4. Atopic Dermatitis

When the skin barrier is compromised, exogenous antigens can penetrate the skin. [25]. The filaggrin gene mutation is one of the causes of skin barrier breakdown. [26] By incorporating this monomer into the lipid envelope, filaggrin plays a crucial role in the stratum corneum for the operation protective barrier of the skin. Moreover, free amino acids are released from filaggrin through extra processing in the top stratum corneum, which helps to maintain the skin's moisture content. [27]. Damage to the skin barrier stimulates the formation of pro-inflammatory cytokines by Langerhans cells and keratinocytes, including IL-33 and thymic stromal lymphopoietin (TSLP), which in turn boosts helper T (Th) 2 immunological responses, which are mediated by IL-12, IL-4, and IL-13. [28] Moreover, interleukin-31 lowers quality of life and quickens itching in atopic dermatitis. [29] The better clinical success for treating atopic dermatitis, cytokine-targeted therapies or restoration barrier function of skin have been devised [30]. The pathophysiology of intrinsic atopic dermatitis involves intrinsic variables despite of external trigger that produces atopic skin inflammation [31]. Patients with intrinsic atopic dermatitis has a constitutionally higher serum nickel concentration than patients with extrinsic atopic dermatitis and persons having good health. [32] Unlike keratinocytes, Toll-like receptor (TLR) 4 is highly expressed in fibroblasts. TLR 4 triggers the production of Interleukin-8 in response to copper and nickel. [33]

2.5. Contact Dermatitis

The sensitization phase plus the elicitation phase are the two stages of the pathophysiology of contact dermatitis [34]. Various inflammatory chemokines and cytokines, including TNF-α and Interleukin 1β are stimulated by external antigens which are exposed to the epidermis during the sensitization phase. This leads to an exaggeration in the activation of cutaneous dendritic cells and an increase intake of antigens to prepare them for migration and maturation into the lymph node drainage. Activated dendritic cells in draining the lymphatic nodules expose naïve T cells to antigens, which trigger effector T cell differentiation and proliferation in the right direction depending on the antigen-specific immune response. Re-exposure to antigens initiates the elicitation phase, causing keratinocyte-derived cytokines to be produced as well as antigen-specific T cell activation and infiltration of the skin spot that was exposed to the antigen. [35] These T cells that are specific to antigens generate inflammatory cytokines, such as interferon (IFN)-γ, which in turn intensify the inflammatory reactions that occur locally. Other immune cells, such as mast cells and Tregs, also are implicated in the pathophysiology of contact dermatitis during both the sensitization and elicitation phases. [36]

3. Prevalence of Skin Conditions

Between 1% and 3% of people have psoriasis, a persistent skin disease for which there is no known treatment. [37]

3.1. Prevalence in Children and Adults

For children, the frequency ranged from zero percent in Taiwan to 2.1% in Italy, but for adults, it varied from 0.91% in the US to 8.5% in Norway. [38]

3.2. Prevalence in Accordance of Sex

If only those with psoriasis who were active during the preceding 12 months were included, the prevalence was 5.0% (n=176). Sex-wise, the prevalence of psoriasis was 8.2% in women and 7.5% in men. 5.3% of women and 4.7% of men in Denmark said they had active psoriasis in the previous year. [39]

3.3. Prevalence Worldwide

Psoriasis is thought to afflict 60 million individuals globally, with 1.52% of the general population in the UK afflicted. [40]

3.4. Prevalence in Developed Countries

The districts with the greatest overall prevalence of skin illness include Anand, Nigeria (39.6%), India (15.41%), Iraq (40.9%), Upper Egypt (86.93%), and Lucknow, North India (42.3%). [41]

3.5. Prevalence in Developing Countries

Research conducted in developing nations has often taken a more inclusive tack, including systematic, community-based surveys supported by analysis. The incidence of skin disorders in underdeveloped nations is estimated to be between 20 and 80 percent. [42]

3.6. Prevalence in Under-Developed Countries

In Ethiopia, the occurrence of skin illness was 61.2%. Roughly 400,000 individuals in Romania suffer with psoriasis, according to the first epidemiological research that was just released in 2021. [43]

4. Cause of Skin Disease

Table 3. Causes of skin diseases.

Disease	Diagnosis	Treatment	Reference
Fungal infections			
Tinea capitis	The most definite test is a culture of lesion scrapings, however quicker findings can be obtained with a potassium hydroxide (KOH) preparation.	The majority of patients have instances that are resistant to treatment, thus systemic antifungal drugs such as terbinafine or other "cidal" antifungal medications like fluconazole, or ketoconazole, itraconazole should be used. Selenium sulfide added to shampoo is advised as an adjunctive treatment.	[44, 45]
Tinea corporis		For circumscribed lesions, topical therapy twice daily with a cidal antifungal drug is useful. Examples of such agents are oxiconazole, ciclopir-	[46]

Disease	Diagnosis	Treatment	Reference
		ox, naftifine, and terbinafine (or more than one of these). Systemic antifungal treatment should be used to treat more diffuse inflammatory disorders.	
Viral infections			
Herpes simplex	The most reliable test, a culture of lesion scrapings, can take several days to complete. Results from a Tzanck smear that detects large cells infected with herpes may be obtained more quickly and precisely.	An oral antiviral drug, such valacyclovir, can be used to treat new, active lesions in order to reduce the length of the infection and lower the risk of transmission.	[47, 48]
Molluscum contagiosum	The diagnosis is made using microscopic examination and clinical data.	Although other anecdotal treatments have been proposed, it is advised to physically destroy the lesions with a sharp curette.	[49, 50]
Bacterial infections			
Impetigo	The history and distinctive look of the lesions are the main factors used in the diagnosis of bacterial infections. Any dubious lesions should yield specimens for culture and antibiotic susceptibility testing.	Treatment for all bacterial infections will depend on the culture and sensitivity of the suspicious lesions. Impetigo has been successfully treated with external fusidic acid (Fucidin H; Leo Pharma, Ballerup, Denmark), mupirocin (Bactroban; GSK, Middlesex, United Kingdom), and retapamulin (Altabax; GSK, Middlesex, United Kingdom).	[51, 52]
Folliculitis/furuncles/carbuncles		Treatment for all bacterial infections depends on the culture and sensitivity of the suspicious lesions.	[53, 54]
Methicillin-resistant Staphylococcus aureus (MRSA)	The history and distinctive look of the lesions are the main factors used in the diagnosis of bacterial infections. i. MRSA is to be included in the differential diagnosis of any possible Staphylococcus lesion. ii. "Spider bite" reported to have been taken seriously as a potential indicator of community-associated MRSA (CA-MRSA). iii. Any suspicious lesions should yield specimens for culture and antimicrobial susceptibility testing.	It is critical to identify and send athletes with questionable lesions. i. Athletes who exhibit questionable lesions ought to be kept apart from their teammates. Local susceptibility data must be used to guide antibiotic treatment decisions, which must be made case-by-case.	[55, 56]

1) Immune system, thyroid, and renal disorders;
2) Environmental triggers, such as allergies or other people's skin;
3) Genetics
4) Drugs used to treat inflammatory bowel illness;
5) diabetes;
6) photosensitivity;
7) heat; sun's ultraviolet radiation [57]

5. Treatment of Skin Diseases

5.1. Treatment of Psoriasis

Table 4. Treatment of psoriasis.

Topical therapy	Systemic therapy (non-biological)	Systemic therapy (biological)	Cytokine inhibitors	Reference
vitamin D analogues	Vitamin D and its analogue	Monoclonal antibodies	Guselkumab	
Coal tar	Acitretin	IgG-fusion proteins	Tildrakizumab	
Dithranol	Etretinate (vitamin A derivative)	Tumor necrosis factor alpha	Ustekinumab	
Retinoid tazarotene		Pro inflammatory cytokines	Brodalumab	[58]
Corticosteroids (tacalcitol or calcitriol)			Ixekizumab	
Desoximetasone			Secukinumab	

5.2. Treatment of Acne

The recommended course of treatment for mild to severe acne is topical therapy. [59] The cornerstones of topical acne treatment include retinoids and antimicrobials such as antibiotics and benzoyl peroxide. These therapies can stop the development of new lesions and are active at the application sites. [60] Local discomfort is the primary adverse effect.

Table 5. Treatment of acne.

Treatment	Reason of use	Research	Reference
Retinoid	Microcomedone is the major target for acne therapy. Retinoid therapy when used topically acts on follicular keratinocytes to prevent excess blockage of cornification and follicle. Additionally, it could decrease the cytokine synthesis that fuels inflammation. Inflammatory lesions and Comedones are reduced by forty to seventy percent with this kind of therapy.	Analyzing five multicenter randomized investigator-blind studies including nine hundred patients, it was shown that 0.1% adapalene gel was more effective than tretinoin 0.025% gel, however it leds to less irritation.	[61] [62]
Topical Antimicrobials	Topical antimicrobials including antibiotics and benzoyl peroxide are effective to treat inflammatory disorders. Benzoyl peroxide, having bactericidal action, prevents P. acnes from becoming resistant to antibiotic therapy. It also has modest anti-inflammatory and comedolytic properties. Many topical preparations ranging in potency from 2.5% to 10.0% are available.	Erythromycin and clindamycin have been shown in several randomized controlled studies to decrease inflammatory lesions by 46% to 70% when applied topically. Most of the time, these drugs are well tolerated.	[63] [64]
Oral antibiotics	250–500 mg of tetracycline twice a day 50–200 mg of minocycline each day 100–200 mg of doxycycline each day 500 mg of erythromycin twice a day 80/400 mg or 160/800 mg of trimethoprim/sulfamethoxazole 4 times a day	After using oral antibiotics for at least six weeks, a response is typically observed. The antibiotics may be progressively stopped and only topical treatment continued if control is maintained for a number of months. Because there is a chance of resistance building, systemic antibiotics shouldn't be used to treat minor cases of acne.	[65] [66]

Treatment	Reason of use	Research	Reference
Hormonal agents	Regardless of the underlying hormonal imbalances, hormonal medications are the second line of therapy for acne. Clinical studies have demonstrated the potential benefits of estrogen-containing oral contraceptives. All formulations are thought to work similarly well, lowering free testosterone levels by boosting sex-hormone-binding globulin. The patient's tolerance and any adverse effects should be taken into consideration while selecting a combination oral contraceptive.	The combination of thirty-five microgram ethinylestradiol and three milligram drospirenone led to a 63% decrease in acne lesions in a randomized controlled research with 128 women, whereas the combination of 35 µg ethinylestradiol and 2 mg cyproterone acetate generated a 59% reduction. Antiandrogen medicine needs to be used for a minimum of three to six months in order to show significant results.	[67] [68]
Isotretinoin	Isotretinoin affects every mechanism that causes acne; it also has anti-inflammatory qualities and corrects abnormal follicular keratinization. Additionally, it prevents P. acnes from colonizing and lowers sebum production by 70%. Isotretinoin is used for a number of conditions, including severe nodulocystic acne, scarring disease, and less than fifty percent effectiveness with oral antibiotics or hormonal therapies after 4 months.	In a 10-year follow-up research including 88 patients, it was discovered that individuals who had cumulatively received isotretinoin between 120 and 150 mg/kg (30%) had a considerably reduced probability of recurrence than patients who had received less than 120 mg/kg (82%).	[69] [70]

5.3. Treatment of Inflammatory Diseases

Table 6. Treatment of acne.

Treatment	Drugs	Reference
Topical	Creams with antibacterial or antifungal properties, lotions containing calamine, creams with corticosteroids to reduce inflammation, and anti-itch creams with hydrocortisone to relieve itching. Immunomodulators, agents that alter the immune system	[71]
Oral	Oral antibiotics and antifungal pills are taken for bacterial infections, while generic antihistamines are provided for some allergic responses.	
Medicinal plants	Flowers of the marigold and chamomile plants, calendula and matricaria, are often used to soothe skin irritation and conditions including dermatitis and eczema. Herbs such as yarrow, aloe vera, witch hazel, and evening primrose oil are also used to treat skin irritation. Herbs with anti-inflammatory properties include purple coneflower sage leaf, ribwort plantain leaf/herb, fenugreek seed, and St. John's wort.	
Alternatives	diet, oil massage, and cold press	

6. Herbal Remedies for Skin Diseases

6.1. Acne

Fruit acids like citric, gluconic, gluconolactone, glycolic, malic, and tartaric acids, offer some potential as topical acne treatments due to their exfoliating properties. In a study, gluconolactone was proved to be more beneficial than a placebo in treating acne lesions that were both inflammatory and non-inflammatory. Even 5% benzoyl peroxide was shown to be effective with it. [72] Especially larger dosages cause irritation which is the common adverse impact of the fruit acids.

Tannins are astringent in nature that's why they are applied topically treating acne. Witch hazel (Hamamelis virginiana) whose bark extract is often made as a home remedy by decocting five to ten grams of plant in one cup (0.24 L) of water. Witch hazel is safe to apply topically. [73] Like astringents, English walnut and white oak tree bark can be employed. These preparations can be used twice or three times a day, but they need to be strained first. [74]

Tea tree oil which also an essential oil is made from the leaves of the small, native species Melaleuca alternifolia in

Australia. There are around a hundred compounds in it, most of which are plant terpenes and the corresponding alcohols. [75] Five percent benzoyl peroxide and five percent tea tree oil in a water-based gel were compared in a study involving 124 participants. Although it did not function as benzoyl peroxide, tea tree oil demonstrated statistical improvement in the acne lesions at the conclusion of three months. Additionally, compared to benzoyl peroxide (79%) tea tree oil had a much reduced occurrence of adverse effects, such as flaky skin, irritation, itching, and burning sensation. [76] It appears that the tea tree oil's monoterpene breakdown products are what cause the skin to become sensitive. Therefore, topical application is thought to be quite safe and effective. [77]

When taken orally, vitex agnus-castus is a helpful remedy for premenstrual acne. The amphoteric hormone-regulating function of the complete-fruit extract is expected to act on the pituitary's follicle-stimulating hormone and luteinizing hormone levels to enhance progesterone and limit estrogen. It can negate the effects of oral contraceptives. According to the German Commission E monographs, 40 mg should be taken daily. The common side effects that have been recorded are rashes and digestive problems. Women who are breastfeeding or pregnant shouldn't take it. [78]

Acne may be improved by bitter herbs that promote acid secretion and other digestive processes. [79] Commission E also approved the oral administration of brewer's yeast (Saccharomyces cerevisiae) and the topical use of bittersweet nightshade (Solanum dulcamara) as the treatment of acne due to its antibacterial qualities. Topical duckweed (Lemna minor) which is used as an acne remedy in China. [78] In China, herbal remedies are also applied topically and orally to cure acne. [80]

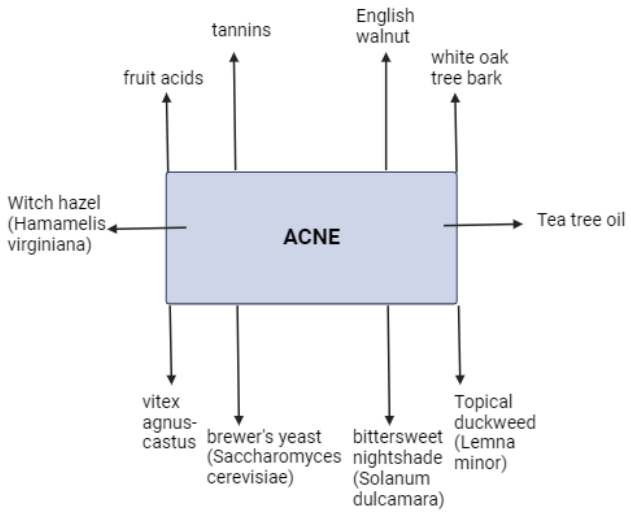

Figure 5. *Herbal treatment of acne.*

6.2. Dermatitis

Arnica montana or other arnica species are the source of arnica, especially their dried flowers. External preparations are quite safe and effective, even if oral administration might pose serious health risks in modest doses. For millennia, people have used arnica, an anti-inflammatory medication, to bruises, bug bites, swollen gums, hemorrhoids, aching muscles, and sore joints. It is also a common element in psoriasis and seborrheic dermatitis treatments. Commission E has given it approval for the topical treatment of skin irritation. [81] To make a compress, mix one tablespoon (tbsp.; fifteen mL) of tincture with 0.5 Liter of water; to make an infusion, mix 2 grams of dried arnica with hundred milliliter of water. In cream or ointment, the amount of arnica oil or tincture should not be more than 15%. [82] The active constituent in arnica include sesquiterpene lactones, which include helanalin, chamissonolid, 13-dihydrohelenalin, and their ester derivatives. These constituents decrease inflammation by lowering the transcription factor nuclear factor κB (NF-κB). The transcriptional regulation of some genes is carried out by the factor NF-κB. These include cytokines such as tumor necrosis factor α, and interleukin (IL)-1, IL-2, IL-6, IL-8, as well as adhesion molecules such as vascular cellular adhesion molecule 1, intercellular adhesion molecule 1, and endothelial leukocyte adhesion molecule 1. It also blocks a great deal of genes that present antigens and cause cyclooxygenase 2 to be activated. [83] It has been reported in some studies that arnica produce contact dermatitis. Additionally, using arnica for longer periods of time or at higher dosages than advised has been reported to cause discomfort on many occasions. It should not be used for application on open wounds or damaged skin. [73]

As it belong to the daisy family, German chamomile (Matricaria recutita) has been used physically and orally for millennia to cure a variety of ailments, including dermatitis, inflammation of the skin or mouth, and symptoms related to the gastrointestinal tract. Two to three teaspoons (tsp; 10 to 15 mL) of dried flowers are added to one cup of water to make a tea that can be consumed or applied topically. In Germany, topical treatments based on cream or ointment are also utilized and studied. [84] Research has indicated that topical chamomile exhibits improvements in contact dermatitis caused by sodium lauryl sulfate and is similar to 0.25% hydrocortisone. [85] In a tiny double-blind experiment, chamomile was shown to considerably reduce wound surface area, and in animal trials, it was also demonstrated to shorten the healing period. Additionally, chamomile has antibacterial properties in vitro. [76] Allergy-induced contact dermatitis is the most common side impact noted. It is regarded as safe for topical and oral usage. [73] German chamomile has anti-inflammatory, antibacterial, and wound-healing properties because of its essential blue oil, which also includes flavonoids, α-bisabolol, chamazulene, and sesquiterpene alcohol. In animal experiments, these compounds exhibited anti-inflammatory and antispasmodic qualities, partly because they inhibited lipoxygenase and cyclooxygenase in vitro. Additionally, the flavonoids function by preventing antigen-

stimulated human basophilic polymorph nuclear leukocytes from releasing histamine. [85] Additionally, α-bisabolol showed that it promoted granulating tissues in the healing of wounds [76]. Brewer's yeast (S. cerevisiae) and bittersweet nightshade (S. dulcamara) are believed to share comparable antibacterial and anti-inflammatory properties.

British researchers have shown that using herbal medication derived from Traditional Chinese Medicine (TCM) to treat atopic dermatitis is successful. Restoring harmony to the body's functioning is the goal of treatment in TCM, which treats the patient as a whole. [86] It is difficult to conduct randomized, controlled research since every patient is given a different mix of many herbs. 2 randomized, placebo-controlled crossover trials were carried out in England to ascertain effectiveness of standardized oral herbal TCM in treating individuals with atopic dermatitis, whose traditional Western treatment had been failed. A standardized combination of 10 herbs, created with assistance from a Chinese physician, can be used to treat atopic dermatitis, a condition marked by erythema, lichenification, and plaques of dermatitis without active exudation or clinical infection. Ledebouriella saseloides, Dictamnus dasycarpus, Clematis armandii, Paeonia lactiflora, Glycyrrhizia glabra, Rehmannia glutinosa, Schizonepeta tenuifolia, Lophatherum gracile, and Dictamnus dasycarpus were the ten plants used. [87] The decoction made from these plants was cooked and given orally as a tea every day in sachet form. The placebo was a concoction of several herbs with comparable tastes and odors that hasn't been shown to be effective in treating atopic dermatitis. In the first research, which involved 37 children, the treatment group's median erythema score decreased by 51.0%, while the placebo group's score improved by just 6.1%. Additionally, the percentage surface participation dropped for the herb-treated and placebo groups by 63.1% and 6.2%, respectively. This preliminary investigation did not reveal any significant negative consequences. Following a year of follow-up, the 37 children were given the option to continue receiving therapy with the TCM herbal mixture. [87] After completing a year of therapy, eighteen children's eczema activity ratings were decreased by 90%. The youngsters who pulled out of the trial did so due to treatment failure, tea's unpleasant taste, or trouble administering the medicine. Seven individuals were able to stop their therapy without experiencing a relapse by the end of the first year. Two individuals had asymptomatic elevations in aspartate aminotransferase levels; these levels returned to normal upon therapy cessation. There were no significant negative effects noted. The other research, which included 31 adult patients having atopic dermatitis, had a similar design. [87] When comparing the herbaceous-treated patients to the placebo group, there was a statistically significant decrease was observed in the erythema and surface damage. Additionally, subjective improvements were noted in sleep and itching. Additionally, these patients underwent a year-long follow-up, during which time they reported no significant side effects and sustained recovery. However, the patients who stopped receiving therapy reported a recurrence in their condition. [73]. The early findings were encouraging patients for whom traditional therapy had been failed, notwithstanding the small sample sizes. The primary constraining factor seems to be the flavor and the method of making the infusion. It is important to highlight that while this study did not reveal any significant side effects, it is nonetheless advised to closely monitor liver function and complete blood cell count because certain TCM have been linked to liver failure and even mortality in cases when baseline laboratory levels did not meet the normal values. [88] It is reported that the specific herbs used in these researches have anti-inflammatory, antihistaminic, antibacterial, antifungal, and immunosuppressive qualities, such as corticosteroids. Some of the ingredients also relax smooth muscles and block platelet-activating factor. Several studies attempted to clarify the mode of action of this ten-plant collection (Zemophyte, manufactured by Phytotech Limited, Godmanchester, England) in the treatment of atopic dermatitis. It has commonly shown that circulating monocytes from individuals with atopic dermatitis display greater amounts of the low-affinity IgE receptor CD23. Studies investigating how aqueous herb extracts affected monocyte's IL-4-induced CD23 expression suggested that CD23 expression could be declining. [89] In a separate study, biopsy specimens of non-lesional skin and lesional skin conditions treated with Zemophyte were compared for immunologic markers for Langerhans cells, T cells, macrophages, and low- and high-affinity IgE receptors. [80] The investigators saw a clinical effectiveness similar to that seen in the previously published Sheehan studies, together with a statistically significant decrease in CD23 antigen-presenting cells. However, the double-blind, randomized, placebo-controlled Zemophyte study was not successfully replicated in Hong Kong to show a statistically crucial benefit of Zemophyte over placebo. [90] A distinct TCM herbal blend called Penta Herbs formula, which has the following components in a ratio of 2:2:2:1:2 were trialed on rat peritoneal mast cells. This Penta Herbs formula consists of root bark of Paeonia suffruticosa; bark of Phellodentron chinensis; flower of Lonicera japonica; aerial portion of Mentha haplocalux; and rhizome of Atractylodes lancea. It is well recognized that this combination helps treat atopic dermatitis clinically. [91] The birch tree bark (Betula platyphylla), which is used for treating atopic dermatitis, was investigated on NC/Nga mice. It reduced skin inflammation, scratching, IgE and IL-4 messenger ribonucleic acid (mRNA) levels, suggesting that it inhibits the T-helper 2 cellular response. [92]

Although research on jewelweed (Impatiens biflora) is inconsistent, it is said to be helpful in treating poison ivy contact dermatitis when used topically. In one study, the use of jewelweed as a therapy for poison ivy contact dermatitis was shown to be equivalent to normal care; in 108 out of 115 patients, the study revealed that the symptoms resolved in two to three days. [93] However, jewelweed extract did not

lessen the symptoms of poison ivy dermatitis in another trial. [94] Another trial revealed no preventive benefit of jewelweed in the management of poison ivy dermatitis. [95] Although the aforementioned studies did not address this element, jewelweed has been reported to work best if administered as soon as feasible following poison ivy exposure. There are no known side effects from topical jewelweed use. [76]

A material known as "mucilage," found in a number of herbs, is helpful topically for calming and emollient effects on skin. Mucilage's found in heartseases (Viola tricolor), marshmallows (Althea officinalis), English plantains (Plantago lanceolata), mulleins (Verbascum thapsus), slippery elms (Ulmus fulva), flax (Linum usitatissimum), and fenugreek (Trigonella foenum-gaecum) are emollients that soothe the skin. When mucilage comes into contact with water, it immediately expands into a sticky substance that helps relieve dry or slightly irritated skin. Mucilage may be worn as a herbal bandage to small wounds and dries as a light adhesive. [78]

Oats (Avena sativa) has calming and antipruritic qualities, when used topically. When it is combined with fluids, colloidal oatmeal transforms into a gooey, sticky substance that may be applied to the skin to lock in moisture, hence, it provides calming and hydrating effect which is linked to the plant's gluten content. Both idiopathic pruritus in the elderly and atopic dermatitis may benefit from this.

An infusion of pansy flowers (V. tricolor hybrids) is advised as a safe remedy for treating seborrheic dermatitis, especially in young children. As a wet treatment, the infusion is prepared by combining one to two teaspoons of flowers with a cup of water. Approximately 0.3% quantities of salicylic acid seem to be the active component. Additionally, it has mucilage and saponins, which have calming and softening properties. Topical application has not been associated with any negative consequences. [76]

Tannins coagulate cell surface proteins and exudates, decreasing secretion and permeability, when used topically to cure dermatitis. Furthermore, a protective barrier is applied to the skin by the precipitated proteins. [85] Tannins potentially have antimicrobial activity. Astringents include tannins found in oak bark (Quercus robur), agrimony (Agrimonia eupatoria), jambolan bark (Syzygium cumini), English walnut leaf (Juglans regia), mullein (Verbascum thapsus), Labrador tea (Ledum groenlandicum), goldenrod (Solidago spp.), yellow dock (Rumex crispus), lady's mantle (Alchemilla spp.), lavender (Lavandula angustifolia), rhatany (Krameria spp.), witch hazel bark (H. virginiana) and St. John's wort (Hypericum montana). Oat straw (A. sativa) is widely known due to its antipruritic and relaxing properties. [84] One study found that in 24 healthy volunteers, 1% hydrocortisone reduced erythema brought on by UV light and cellophane tape peeling more effectively than extract of witch hazel in a phosphatidyl choline basis. [96]. In a clinical trial with two groups—one with atopic dermatitis (n = 36) and the other with contact dermatitis (n = 80)—extract of witch hazel was compared with control group. In the atopic group, witch hazel showed marginally greater results in lowering inflammation and irritation. Anecdotal evidence indicates that atopic dermatitis may benefit from the use of witch hazel. [85]

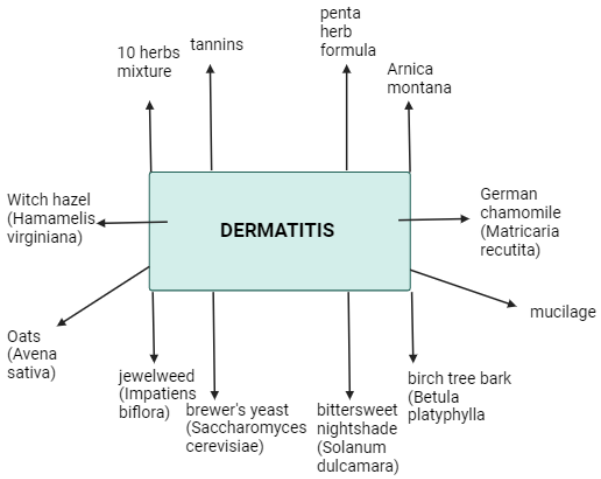

Figure 6. *Herbal treatment of dermatitis.*

6.3. Bacterial and Fungal Infections of Skin

Ajoene, a compound found in garlic called as Allium sativum, has been shown to have antifungal properties. 34 patients with tinea pedis who received a daily topical treatment of 0.4% ajoene cream reported 79% of their symptoms clearing up in 7 days, while the remaining patients reported clearing up in 14 days. After three months, none of the individuals had any fungal infections. [97] Isolated cases of contact dermatitis with repeated topical exposure have been reported. [98] When garlic is used orally, prolonged bleeding might happen [78].

Tea tree oil is beneficial to treat bacterial and fungal infections when applied topically. Numerous microorganisms have been shown to be sensitive to the antibacterial properties of tea tree oil in vitro, including Staphylococcus aureus, Propionibacterium acnes, Escherichia coli, Trichophyton mentagrophytes, Candida albicans, and Trichophyton rubrum. [99] In a double-blind, randomized study, ten percent tea tree oil cream was given to one hundred and four patients while one percent tolnaftate cream and a placebo cream were given to the same patients. Comparable degrees of symptomatic relief were reported by the tolnaftate and tea tree oil groups; on the other side, the tolnaftate treated group had a much larger mycologic cure (85%) than the tea tree oil treated group (30%). There was no discernible difference in the rates of cure between the groups who received tea tree oil and the placebo. [100] In a different randomized, double-blind study, a hundred percent tea tree oil was used as solution and a one percent clotrimazole solution were compared

for the treatment of onychomycosis in 117 patients. The mycologic cure rates eleven percent for clotrimazole and eighteen percent for tea tree oil was seen after six months of therapy, as were clinical observations and subjective evaluations of signs and symptoms (sixty one percent for clotrimazole and sixty percent for tea tree oil). [101] Thus, symptomatically, tea tree oil may be helpful in healing superficial wounds like tinea pedis and onychomycosis. However, it shouldn't be used on burns due to its cytolytic effect on fibroblasts and epithelial cells. [102]

Applying thyme oil (Thymus vulgaris) topically has been used as an antibacterial and anticandidal treatment. [103] It was discovered that a methanol extract from the traditional Korean antifungal plant Galla rhois proved beneficial against Candida albicans [104].

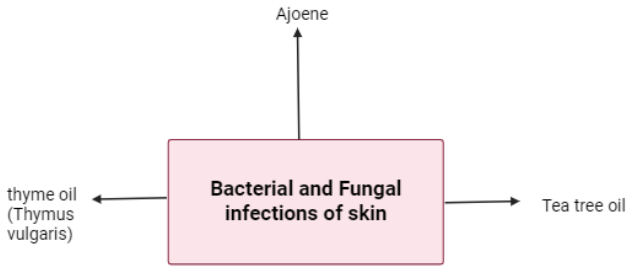

Figure 7. *Herbal treatment of bacterial and fungal skin conditions.*

6.4. Psoriasis

Aloe vera (Aloe vera) has been used for generations to heal wounds, and it was recently shown to have potential as a psoriasis therapy. In a double-blind, placebo-controlled study, sixty people having mild to severe plaque based psoriasis were given topical therapy with either 0.5% hydrophilic aloe cream or a placebo. The group that received aloe treatment showed statistically significant alleviation in symptoms (83.3%) in comparison to the placebo group (6.6%). No adverse effects were reported in the treatment group. [105]

Capsaicin, the active constituent in cayenne pepper (C. frutescens), which has been studied as a possible treatment for psoriasis. It was shown that capsaicin prevented phorbol ester-produced transcription factors NF-κB and AP-1 from activating in vitro. [106] 2 trials showed that 0.025% cream which is used topically can successfully cure psoriasis. Over a six-week period, 44 participants with moderate to severe psoriasis showed significant reduction in erythema and scaling. [107] In the second, 197 patients received four daily doses of capsaicin cream as part of a double-blind experiment that lasted six weeks. The findings demonstrated a significant decrease of erythema, scaling, thickness, and itching [108]. A short period of burning sensation at the site of application was the main negative effect that was reported. Using capsaicin in close contact to the eyes or on wounds is not advised. Furthermore, the German regulator Commission E states that it should not be used more than twice in consecutive days, with a 14-day break between applications. A patient survey at a well-known university of dermatology clinic revealed that fifty one percent of patients with psoriasis reported utilizing one or more alternative therapy methods. [109] This is in line with earlier Norwegian research on psoriasis sufferers. [110] One of the most popular supplementary therapies is herbal therapy. Herbal remedies have been used topically and internally to treat psoriasis for millennia. Furocoumarins, the main component of many herbal treatments, function as psoralens when paired with UVA (ultraviolet (UV) A, 320–400 nm). Furocoumarins from the species Ammi majus and allied plants intercalate with DNA when applied topically or swallowed to create 8-methoxypsoralen. Moreover, the photoactivation creates cross-links with the thymine in the DNA when combined with exposure to UV-A from the sun or an ultraviolet light box, which results in cell death. [111] Thus, hyper proliferation in psoriatic lesions is inhibited.

Radix Angelicae dahurica, a popular TCM, includes imperatorin, isoimperatorin, and alloimperatorin, three furocoumarins. This TCM was given orally in conjunction with UV-A therapy in a research involving 300 patients who had psoriasis. The results were compared with the usual psoralen treatment, which used UV-A mixed with methoxsalen. The two therapies were equally effective, however the group receiving TCM and UV-A experienced less side effects such nausea and vertigo. [112] Furthermore, topical herbal treatments having systemic effectiveness in treating psoriasis are hazardous when administered systemically. [113] Topical TCM with the herb Camptotheca acuminata was shown to be statistically more beneficial than one percent hydrocortisone in an open investigation involving ninety-two psoriasis patients. The disadvantage was that nine to fifteen percent of the patients in the TCM group experienced allergic contact dermatitis. It is challenging to compare TCM combinations in clinical trials since the specific herb combination advised varies according on the subgroup of psoriasis (e.g. "blood-heat," the blood insufficiency, dryness, and "blood stasis" sorts). This subtype in TCM is identified by several features, such as the pulse, psoriasis lesions, and tongue condition. [114]. Certain forms of TCM may have some effect on the psoriatic lesion's microcirculation [115]. Below is a collection of other TCM herbal remedies for psoriasis [116].

Turmeric (Curcuma longa), has around 5% curcumin. India has been using turmeric for ages to give skin a radiant, glossy appearance. Its beneficial properties include antibacterial, antioxidant, astringent, and others that aid in wound healing and scar reduction. [117] It has been found that activated transcription factors NF-κB and AP-1 produced by phorbol ester is inhibited by the pure turmeric extract curcumin in-vitro. [118] Phosphorylase kinase activity decreases in response to topically applied curcumin to lesions and psoriasis remission follows. [119] Because to its microencapsulation, curcumin is more bioavailable and leaves the skin less

stained yellow when applied topically. [120]

Tars have long been used as a psoriasis treatment. Tars derived from trees such as beech (Fagus spp.), birch (Betula spp.), and juniper (Juniperus spp.). [121] They are both antipruritic and antiproliferative, when they are added in concentration of 5–10% to creams, gels, and soaps. They can be used in conjunction with UV-B (250–320 nm) or narrow banded UV-B (311 nm) light since they are photosensitizing materials. Relatively little sun exposure can also be beneficial.

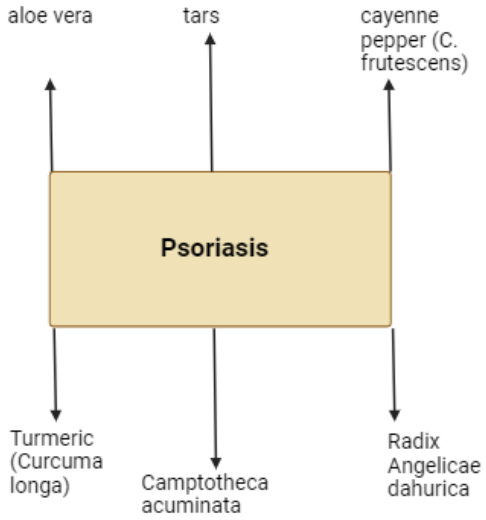

Figure 8. *Herbal treatment of psoriasis.*

7. Use of Thymoquinone for Cure of Skin Conditions

Utilizing imiquimod-induced psoriatic plaque model and in vitro cell lines, the anti-psoriatic and anti-inflammatory potential of thymoquinone was ascertained. [122] Thymoquinone, resveratrol, and curcumin are three possible natural bio active's shown to have strong anti-psoriatic effects. These natural bio actives have low water solubility and good skin penetration. TQ-loaded extracellular vesicles were made using a cold technique and they were evaluated for a number of critical characteristics including flexibility, morphology, percent drug entrapment, rheological and textural characterization and skin absorption. Using a mouse-tail model for psoriasis, the optimal formulation was ultimately assessed for anti-psoriatic efficacy on Swiss albino mice. [123] TQ is a naturally occurring bio-active compound that has anti-psoriatic properties. [124] According to studies, thymoquinone can control a wide range of signaling pathways including mitogen-activated protein kinase (MAPK) at the molecular level, nuclear factor kappa beta (NF-κβ), tumor necrosis factor-α (TNF-α), janus kinase/signal transduction and activator of transcription (JAK-STAT), oxidative stress, regulatory T cells, interleukins and epigenetic modification. [125] Given their immunomodulatory, anti-inflammatory qualities as well as their antioxidant, antimicrobial, antineoplastic, and other activities, N. sativa and TQ have been useful therapeutic preparations for treating a range of infectious and noninfectious skin conditions such as vitiligo, cancer, autoimmunity, and various types of allergies. [126] NS has demonstrated efficacy lately in treating psoriatic lesions. [127]

Table 7. *Thymoquinone and its mechanism of action.*

Drug or combination of pharmaceutical agents	Mechanism of action	Result	Reference
Nigella sativa, methotrexate and their combination	An imbalance between the oxidant and anti-oxidant systems is seen in psoriasis. There is antioxidant action in Nigella sativa. In addition to oxidative stress, methotrexate can also inhibit T-cell activation; reduce cell proliferation, and antagonistic effects on folate.	Methotrexate alone has a greater effect than nigella sativa alone, but the combination had the biggest impact.	[128]
Nigellia sativa	Patients are happier with the ointment since they find its nice aroma and the fact that it doesn't ruin or stain clothing. As with other recipes for ointments, when applied topically, oil in ointment distributes active components straight into the lesion at the application site than other routes of delivery. In fifty percent (50%) of the instances, the crude powder in the form of capsules (500 mg three times daily) improved the psoriatic lesion. Compared to therapy with either the ointment or the combination, the beginning of effect was delayed. Patients did not enjoy capsules because most of them thought that topical treatments, as opposed to oral	Nigella sativa has antipsoriatic properties, and the optimum results are achieved when the ointment and oral dosage form are combined.	[129]

Drug or combination of pharmaceutical agents	Mechanism of action	Result	Reference
	ones, were a superior way to treat skin conditions like psoriasis.		
Thymoquinone	Thymoquinone has anti-oxidant, pro-apoptotic, chemoprevention, anti-inflammatory action.	Through a variety of mechanisms of action, thymoquinone has shown therapeutic benefits in the treatment of inflammation and cancer. Research indicates that this substance has strong anti-free radical and superoxide radical scavenging properties while securing the properties of several antioxidant enzymes, including glutathione-S-transferase, catalase, and glutathione peroxidase.	[130]
Thymoquinone	Its anti-inflammatory and anti-oxidant actions are produced via activating cyclooxygenase-2 (COX2), phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT), nuclear factor erythroid 2–related factor 2 (Nrf2), and nuclear factor kappa–light-chain–enhancer of activated B (NF-Kβ).	Has been demonstrated to lower various pro-inflammatory cytokines and ROS.	[131]
Thymoquinone	Nigella sativa is a widely used plant for medicinal properties having a rich cultural and religious past in Unani, Ayurvedic, Chinese, and Arabic medicine. Alkaloids, saponins, thymoquinone, and alpha-hederin are some of the naturally occurring bioactive chemicals that provide N. sativa its many health advantages, which include bronchodilator, diuretic, antihypertensive, antidiabetic, and analgesic properties. Moreover, N. sativa demonstrates antibacterial, reducing inflammatory, and antineoplastic activity, which make it a strong therapeutic choice for the treatment of skin conditions.	The application of N. sativa extract having antibacterial, anticancer, antioxidant, and reducing inflammatory response in the treatment of dermatological disorders, is backed by a large body of scientific research.	[132]
Thymoquinone	Prior to receiving Nigella Sativa oil, the majority of teenagers with acne vulgaris had serious skin integrity issues. Adolescents with acne vulgaris experienced minor skin integrity disorder following the treatments.	Adolescents with acne vulgaris who receive Nigella Sativa oil administration show improvement in skin integrity.	[133]

8. Challenges

Psoriasis is a chronic public health issue that affects around 125 million people worldwide. [134] According to estimates, the frequency among adult populations ranges from 8.5% in Norway to 0.91% in the United States of America (U.S.A.). Globally, the cases increased in number from 758/100,000 in 1990 to 812/100,000 in 2017. The European area has the greatest incidence rates; that was recorded to rise the incidence from 143.7 cases per 100,000 in 1990 to 147.2 cases in 2017. [135]

The inflammatory processes linked to the systemic aspect of psoriasis may go unnoticed, and co-morbidities may have a substantial unwanted influence on a quality of life of patient and overall health. [136]

It can appear at any age and is persistent and incurable. The illness is marked by erratic remission and recurrence times. [137]

Diabetes, psoriatic arthritis, and cardiovascular disease are among the comorbidities that are more common in people with psoriasis and increase the risk of early mortality. It can also have a detrimental effect on patient's relationships, productivity, and professions. It is linked to anxiety, sadness, and social isolation. [138]

There are now more therapy alternatives than ever before

for psoriasis. However, as it is impossible to anticipate which patient will respond to a certain medication, doctors sometimes have difficulty deciding which systemic or biologic medicine to start for their patient. From the perspective of the patient and the socioeconomic system, the ensuing primary and subsequent treatment failures are expensive. [139] Patient-reported outcomes (PROs) are being used to put more of a focus on HRQoL because the main goal of any treatment is to lessen the patient's burden. But existing PROs, such the Dermatology Life Quality Index (DLQI), which measure how a disease affects HRQoL, have a narrow focus and do not specifically address psoriasis. [140]

Patients who have difficulty using topical therapies may benefit more from recent developments in systemic therapy. Results on the effectiveness and safety of systemic treatment (conventional or biological) for the management of psoriasis in difficult-to-treat areas were obtained from scarce-controlled studies. Majority of the information that is currently available comes from sub-analyses of studies that included individuals with psoriasis and/or PsA along with an evaluation of the nails, scalp, palms, and soles that were affected. [141]

In the last ten years, there have been advancements in treatment approaches and medications, particularly for those with moderate-to-severe disease types. Biologics, in the middle of these recently created medications, guarantee the specific immune-mediated pathway suppression through cytokines, such as IL-17, IL-36, interleukin 23 (IL-23), and tumor necrosis factor (TNF). Despite these developments, psoriasis is still not always treated to its best potential; patient satisfaction with current medicines is still low; and the disease burden is still high despite the efficacy of new treatments. [142]

8.1. Use of Thymoquinone to Cope Up with the Challenges

The majority of people on the planet rely on herbal treatments for medical care because they think they pose less health risks. The World Health Organization concurs that using herbal treatments in the contemporary world is growing daily. Worldwide, Nigella sativa (N. sativa), often known as black-caraway or "Kalonji," is a highly prized seed. One of the most sought-after medicinal plants in the world, its fixed oil includes beneficial chemical components such as nigellimine, nigellicine, carvacrol, nigellidine, thymoquinone, dithymoquinone, thymol, and alpha-hederin. It has been discovered to have a broad variety of pharmacological actions that are advantageous for numerous body areas because of the availability of helpful components. These benefits include the ability to heal wounds and possess antibacterial, antiviral, and anti-inflammatory qualities. They also include applications for skin cancer, pigmentation, acne vulgaris, and a variety of cosmeceutical purposes. According to custom, N. sativa oil and seeds are utilized in a wide range of culinary and medicinal systems. [143]

Nigella sativa is a Mediterranean native that blooms annually and is native to Pakistan and India, which is member of the Ranunculaceae family. It is a little shrub with rosaceous white and violet blooms and tapering green leaves. There are little, dark-black seeds in the fruit. [144]

N. sativa seeds include proteins, saponin, alkaloids, 36-38% fixed oils, and 0.4–2.5% essential oil. [145] Studies using High Performance Liquid Chromatography (HPLC) have shown that thymoquinone (TQ), thymol (THY), dithymoquinone (DTQ), and thymohydroquinone (THQ) are the main active ingredients of NS. [145]

Numerous pharmacological properties of TQ have been demonstrated, indicated as

1) anti-oxidant
2) reduce inflammation
3) anti-tumor,
4) anti-histaminic,
5) immunomodulatory, and
6) anti-microbial
7) Actions that are neuroprotective, hepatoprotective, gastro protective, and nephroprotective.
8) Positive results have also been demonstrated in the treatment of fibrosis and bone problems, as well as in the management of diabetes, reproductive disorders, respiratory conditions, and cardiovascular illnesses.
9) Furthermore, a substantial body of research indicates that TQ has very few side effects and no significant toxicity. [121]

8.2. Thymoquinone in Homeopathic Products

Table 8. Homeopathic dosage forms containing thymoquinone.

Name of product	Dosage form
Mother tincture	Tincture containing thymoquinone
Thymolum	Tincture
Al hawang cream	Cream
Black seed miracle skin repair	Cream

Name of product	Dosage form
Planta elcaptain (elcaptain ointment with black seed)	Ointment
Black cumin containing 2-2.4% thymoquinone	Suspension for allergy symptoms

9. Treatment Approach Using Thymoquinone

Since N. sativa seed oil and TQ are classified as pan-assay interference compounds, research on both humans and animals suggests that they may have a role in a variety of disease conditions, such as elevated blood pressure, dyslipidemia, diabetes mellitus type 2, asthma, arthritis, bacterial and viral infections, neurological disorders, and skin disorders. [120]

This discovery demonstrated that TQ had anti-inflammatory qualities that inhibit the manufacture of crucial mediators involved in inflammatory processes and asthma, including COX, 5-LO, PGD2, and LTs. TQ also decreased proinflammatory cytokines generated by Lipopolysaccharide, including TNF-α and interleukins (ILs). TQ also shown to have immunomodulatory function in humoral and cellular immunity. [122]

Human skin carcinogenesis has been shown to involve aberrant expression of COX-2. Consequently, it has been revealed that thymoquinone inhibit aberrantly activated inflammatory signaling pathways and induce cytoprotection against oxidative stress by inducing cytoprotective proteins having chemopreventive benefits against cancer. [121]

Topical administration of N. Sativa oil extract have wound-healing benefits in rabbit models with cutaneous wounds, as evidenced by the production of granulating tissue, fibroblast proliferation, angiogenesis and collagen preparation. [126] The ability of Nigella sativa aqueous extract to heal wounds was examined using an in vitro model with human gingival fibroblast monolayer. It was discovered that the extract scavenges free radicals, promotes fibroblast proliferation, increases wound closing activity, and raises basic Fibroblast Growth Factor (bFGF) levels. [127]

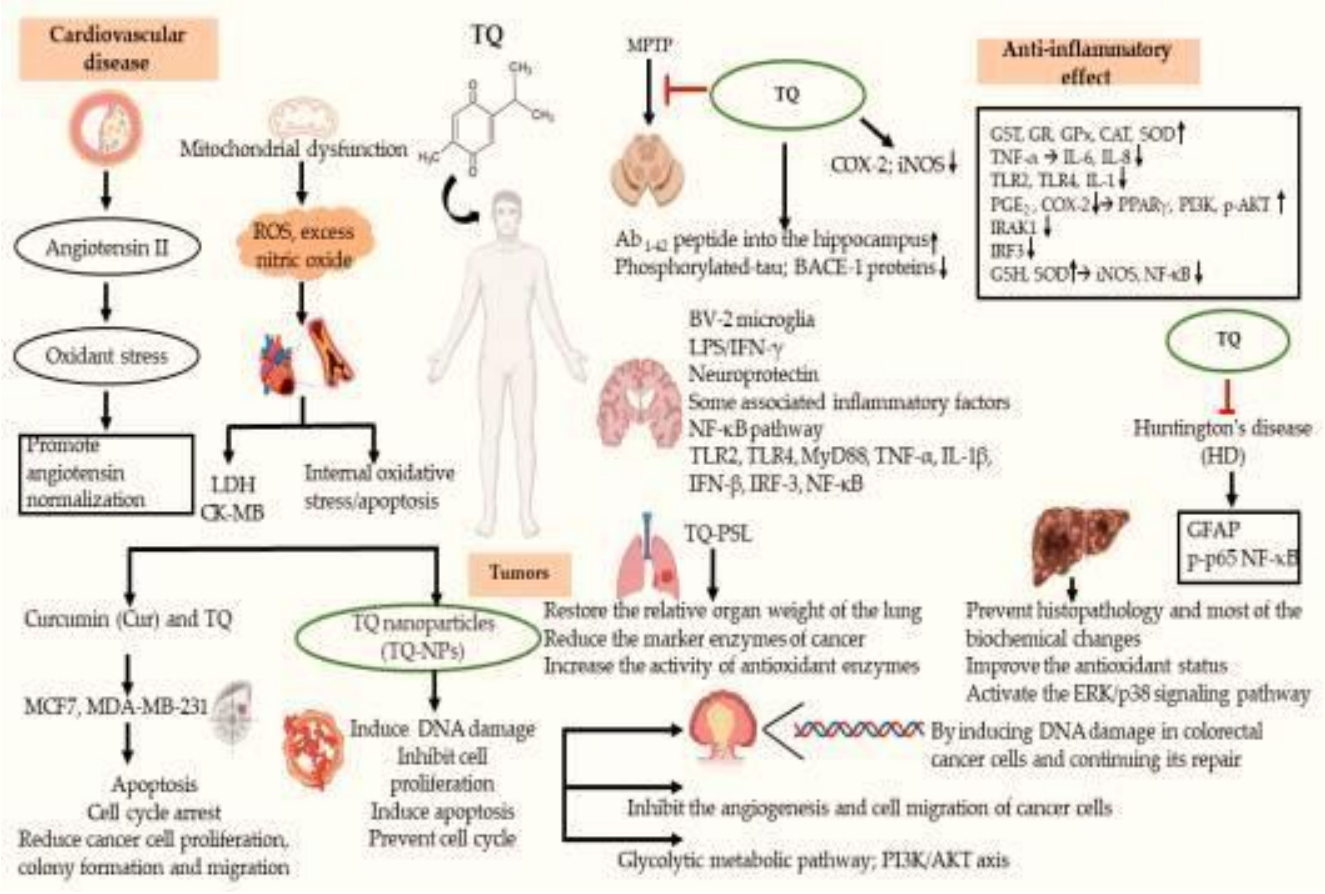

Figure 9. *Thymoquinone in Inflammatory conditions [128].*

9.1. Thymoquinone and Hydrocortisone Benefits in Skin Conditions

Table 9. Thymoquinone and hydrocortisone mechanism of action.

Constituent	Activity	Mechanism of action	Reference
Thymoquinone	Anti-inflammatory and anti-oxidant	Prevent COX2 inhibiting prostaglandins from being expressed. Reduces certain pro-inflammatory regulators such as interleukin 6 (IL-6), interleukin 1 beta (IL-1β), tumor necrosis factor (TNFα), prostaglandin E2 PGE (2), and interferon γ (IFNγ).	[124]
Hydrocortisone	Anti-inflammatory and anti-itch agent	Exert biological effects by binding to the glucocorticoid receptor. Glucocorticoid receptor complex is formed, DNA binding site of receptor exposed and absence of inflammatory response occurs because of alterations in translation and transcription of proteins.	[129]

9.2. Previously Established Dosage Forms of Thymoquinone

Topical administration techniques have several benefits since they minimize systemic negative effects and provide a localized impact. [130] Solid lipid nanoparticles, nanostructured lipid carriers, liposomes, noisome, transferases, ethosomes, and other different carriers are mostly employed for topical distribution. Their tiny globule size and lipidic nature allow them to give significant medication loading and holding onto the skin. Theoretically, by removing and expanding skin lipids, a Nano emulsion can boost pore penetration and more effectively penetrate the resistant plaques on psoriatic skin. Moreover, it is easy to compress thymoquinone into gel form, which enhances drug retention in the skin and facilitates the hydration-mediated delivery of drugs into the skin. [131]

Nevertheless, since Nano emulsions have globule diameters between 20 and 200 nm and are the simplest, transparent, and kinetically stable systems, using them as topical drug delivery systems is a feasible approach. [133] Self-emulsifying formulations based on lipid surfactants are consistently the preferred option for addressing the constraints and unpredictable oral bioavailability of lipophilic medicaments that are poorly soluble in water. [139]

Self-nanoemulsifying drug delivery systems (SNEDDS) are a more popular self-emulsifying formulation system due to their demonstrated ability to reduce incomplete and slow drug dissolution and speed up the formation of the drug's highly potent solubilized phase for systemic absorption. [130]

SNEDDS, which can solidify into solid form, is primarily a liquid isotropic mixture of active medicinal medication in a mixture of lipids, surfactants, and water soluble co-solvents. [146] Thymoquinone, resveratrol, and curcumin are three possible natural bio actives that have been shown to have strong anti-psoriatic effects. These natural bio actives have low water solubility and good skin penetration. The creation and development of Nano-emulsion gel formulation for the simultaneous administration of these 3 medications is the main focus of current research efforts in this respect. PEG 200 which is used as a co-surfactant, Tween 20 acts as surfactant and oleic acid serves as the oil phase in the NE system. [145]

10. Conclusion

There aren't many prescription creams on the market that include thymoquinone and hydrocortisone, despite their known therapeutic advantages for dermatological disorders like psoriasis, eczema, and acne. Patients' options and convenience are limited by the fact that most existing formulations are in the form of gels or ointments. Furthermore, although thymoquinone pharmacological characteristics have been well investigated, little is known about how it might be included into topical formulations, especially creams.

Furthermore, due to worries about the safety and adverse effects of synthetic medications, there is a rising market for natural and herbal therapies in cosmetics. Thymoquinone's source, Nigella sativa, has a long history of traditional usage in many medical systems, which highlights the potential benefits of formulations containing thymoquinone for skin health.

Thus, the main goal of this research is to close the market gap by creating a medicinal cream that contains hydrocortisone and thymoquinone. With the use of hydrocortisone and thymoquinone's synergistic effects, this cream seeks to provide patients with a quick and efficient means of treating common dermatological disorders. This review article aims to demonstrate the effectiveness of thymoquinone containing creams in clinical practice and promote dermatological treatment via thorough formulation development and rigorous assessment.

Thymoquinone functions to reduce inflammation and is used to treat psoriasis patients. We are adding hydrocortisone, a steroidal drug, to TQ in order to increase its stability, efficacy, intensity, and duration of action, since research has showed that TQ has reduced permeability through the skin.

Millions of people worldwide suffer from dermatological disorders including psoriasis, eczema, and acne, which can cause pain, discomfort, and psychological misery. There is still a need for efficient and well-tolerated topical formulations that can address these problems, even with the abundance of therapeutic choices. A bioactive substance called thymoquinone, which is extracted from Nigella sativa seeds, has shown encouraging pharmacological qualities, such as reducing inflammation, antioxidant, and wound-healing capabilities. Thymoquinone and hydrocortisone, a well-known anti-inflammatory drug, together may improve topical formulations' therapeutic effectiveness for dermatological diseases.

Although thymoquinone-based formulations are available as gels and ointments, prescription creams containing thymoquinone are conspicuously lacking. Compared to other dosage forms, creams provide a number of benefits, such as patient preference, quick absorption, and convenience of application. Filling this market void can provide patients a practical and efficient course of therapy. Formulations using plant extracts like thymoquinone are becoming more and more popular as people's interest in natural and herbal skincare solutions grows. Using thymoquinone's inherent healing qualities in a cream formulation satisfies customer demands for more sustainable and safe skincare products. Though thymoquinone's pharmacological characteristics have been studied in great detail, its use into medicinal creams has not received as much attention. Examining the preparation and assessment of a thymoquinone and hydrocortisone cream might yield important information for the dermatological pharmacotherapy community.

Abbreviations

cp	Centipoise
cm	Centimeter
HLB	Hydrophilic Lipophilic Balance
SC	Stratum Corneum
O/W	Oil in Water Emulsion
W/O	Water in Oil Emulsion
O/W/O	Oil in Water in Oil Emulsion
W/O/W	Water in Oil in Water Type Emulsion
FDA	Food and Drug Authority
RPM	Revolution Per Minute
TQ	Thymoquinone
HC	Hydrocortisone
COX2	Cyclooxygenase
N. sativa	Nigella Sativa
g	Gram

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Author Contributions

Faizan Hamid: Conceptualization, resources, Data curation, Funding acquisition, Investigation, Project Administration, Supervision, validation, visualization

Ayesha Hamid: Methodology, Formal Analysis, Investigation, writing-original draft, writing-review and editing Referencing

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Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] M. D, "Surfactant Science and Technology, VCH Publishers," p. 209-247, 1992.

[2] P. A. Kolarsick, "Anatomy and Physiology of the Skin".

[3] N. D. Bikiaris, "Preparation and Investigation of the SPF and Antioxidant Properties of O/W and W/O Emulsions Containing Vitamins A, C and E for Cosmetic Applications," MDPI, 2023.

[4] " Skin Anatomy, Physiology, and Healing Process ".

[5] D. Palmer, "Skin Anatomy, Physiology, and Healing." Physiotherapy Wound Care Programme. Plus. 2022.

[6] L. D. L. N. Piipponen M, "The immune functions of keratinocytes in skin wound healing." International journal of molecular sciences. 21 1 2020.

[7] M. S. Abraham J, "Merkel cells: a collective review of current concepts." International Journal of Applied and Basic Medical Research, 2019.

[8] R. a. Wilson, “Anatomy and Physiology in Health and Illness".

[9] "Matsui, T. (2023). Epidermal barrier development via corneoptosis: a unique form of cell death in stratum granulosum cells. Journal of Developmental Biology, 11(4), 43.

[10] Y. T. W. J. S. J. B. D. Soliman AM, “Isolation of Skin Leukocytes Uncovers Phagocyte Inflammatory Responses During Induction and Resolution of Cutaneous Inflammation in Fish.” Frontiers in Immunology. 2021.

[11] C. Lalita, "Creams: A Review on Classification, Preparation Methods, Evaluation and its Applications,” Journal of Drug Delivery and Therapeutics, 2020.

[12] H. RJ, "The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions.” 2014.

[13] F. A. Wagener, “Targeting the redox balance in inflammatory skin conditions,” 2013.

[14] A. Rendon, "Psoriasis Pathogenesis and Treatment,” national library of medicine, 2019.

[15] S. H. Ibrahim, "Systemic Immune Inflammatory Index Is Associated with Pustular Psoriasis: A Single Center Retrospective Study,” Journal of Cosmetics, Dermatological Sciences and Applications, vol. 12, 2022.

[16] A. Rendon, "Psoriasis Pathogenesis and Treatment,” international journal of molecular science, 2019.

[17] C. Albanesi, "Immunology of Psoriasis,” science direct, 2019.

[18] A. W. Armstrong, "Psoriasis Prevalence in Adults in the United States,” JAMA dermatology, 2021.

[19] N. Kanda, "Nutrition and Psoriasis,” MDPI, 2020.

[20] G. Egawa and K. Kabashima, “Barrier dysfunction in the skin allergy."

[21] C. palmer, A. Irvine, A. Terron-Kwiatkowski, Y. Zhao, H. Liao, S. Lee, D. Goudie, A. Sandilands, L. Campbell, F. Smith and e. al. "Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis.” 2006.

[22] J. thyssen and S. Kezic, "Causes of epidermal filaggrin reduction and their role in the pathogenesis of atopic dermatitis.” 2014.

[23] S. Nakajima, T. Nomura, J. Common and K. Kabashima, "Insights into atopic dermatitis gained from genetically defined mouse models.” 2019.

[24] A. Otsuka, M. Tanioka, Y. Nakagawa, T. Honda, A. Ikoma, Y. Miyachi and K. Kabashima, “Effects of cyclosporine on pruritus and serum IL-31 levels in patients with atopic dermatitis.” 2011.

[25] L. Beck, D. Thaçi, J. Hamilton, N. Graham, T. Bieber, R. Rocklin, J. Ming, H. Ren, R. Kao, E. Simpson and e. a. Dupilumab, “Treatment in Adults with Moderate-to-Severe Atopic Dermatitis.” 2014.

[26] Y. Tokura, “Extrinsic and intrinsic types of atopic dermatitis.” 2010.

[27] H. Yamaguchi, N. Hirasawa, S. Asakawa, K. Okita and Y. Tokura, "Intrinsic atopic dermatitis shows high serum nickel concentration.” 2015.

[28] V. Frings, D. Müller, G. Storz, A. Rossi, H. Sennefelder, C. Adam, M. Goebeler, F. Groeber-Becker and M. Schmidt, “Improved metal allergen reactivity of artificial skin models by integration of Toll-like receptor 4-positive cells.” 2019.

[29] Y. Sawada, T. Honda, S. Hanakawa, S. Nakamizo, T. Murata, Y. Ueharaguchi-Tanada, S. Ono, W. Amano, S. Nakajima, G. Egawa and e. al. "Resolvin E1 inhibits dendritic cell migration in the skin and attenuates contact hypersensitivity responses.” 2015.

[30] Y. Natsuaki, G. Egawa, S. Nakamizo, S. Ono, S. Hanakawa, T. Okada, N. Kusuba, A. Otsuka, A. Kitoh, T. Honda and e. al, "Perivascular leukocyte clusters are essential for efficient activation of effector T cells in the skin.” 2014.

[31] T. Honda, G. Egawa, S. Grabbe and K. Kabashima, “Update of Immune Events in the Murine Contact Hypersensitivity Model: Toward the Understanding of Allergic Contact Dermatitis.” 2013.

[32] L. Parrish, "Psoriasis: symptoms, treatments and its impact on quality of life,” british journal of community nursing, vol. 17, 2013.

[33] P. R, "Global epidemiology of psoriasis: a systematic review of incidence and prevalence.” journal of investigative dermatology, 2012.

[34] A. Egeberg, "Prevalence and characteristics of psoriasis in Denmark: findings from the Danish skin cohort,” BMJ journals, vol. 9.

[35] A. M. Dessie, "Prevalence of Skin Disease and Its Associated Factors Among Primary Schoolchildren: A Cross-Sectional Study from a Northern Ethiopian Town,” pub med, 2022.

[36] R. Hay, "Disease Control Priorities in Developing Countries.” pub med.

[37] A. C. Nicolescu, "Prevalence and Characteristics of Psoriasis in Romania-First Study in Overall Population,” PUB MED, 2021.

[38] D. W. Pleacher MD, "Cutaneous fungal and viral infections in athelets,” 2007.

[39] B. RS. "Skin problems in athletics.” 2002.

[40] M. D. B. M. Kohl TD, "Comparison of topical and oral treatments for tinea gladiatorum.” 1999.

[41] J. R. W. K. e. Fitzpatrick TB, “Cutaneous Fungal infections,” 1997.

[42] A. BB. "New strategies for the diagnosis, treatment, and prevention of herpes simplex in contact sports.” 2004.

[43] B. R. Rogers M, "Diseases of the skin.” 1998.

[44] O. D. Ross GL, "Combination topical treatment of molluscum contagiosum with cantharidin and imiquimod 5% in children: a case series of 16 patients." 2001.

[45] A. BB. "Sports dermatology." 2001.

[46] V. A. Koning S, "interventions for impetigo," 2004.

[47] Chayavichitsilp, P., Buckwalter, J. V., Krakowski, A. C., & Friedlander, S. F. (2009). Herpes simplex. Pediatrics in review, 30(4), 119-130.

[48] L. FD. "Staphylococcus aureus infections." 1998.

[49] M. M. H. C. Rihn JA, "Community-acquired methicillinresistant Staphylococcus aureus: an emerging problem in the athletic population," 2005.

[50] G. S. K. S. E.-G. E. L. E. Postier RG, "results of a multicenter, randomized, open-label efficacy and safety study of two doses of tigecycline for complicated skin and skin-structure infections in hospitalized patients," 2006.

[51] "Hartman-Adams, H., Banvard, C., & Juckett, G. (2014). Impetigo: diagnosis and treatment. American family physician, 90(4), 229-235.

[52] K. D. L. J. e. a. Strauss JS, "Guidelines of care for acne vulgaris management." 2007.

[53] Dawson, A. L., & Dellavalle, R. P. (2013). Acne vulgaris. Bmj, 346.

[54] S. J. Haider A, "Treatment of acne vulgaris." JAMA, 2004.

[55] P. M. L. C. e. a. Cunliffe WJ, "A comparison of the efficacy and tolerability of adapalene 0.1% gel vs tretinoin 0.025% gel in patients with acne vulgaris: a meta analysis of five randomized trials." 1998.

[56] N. J. C. W. Hughes BR, "A double-blind evaluation of topical isotretinoin 0.05%, benzoyl peroxide gel 5% and placebo in patients with acne." 1992.

[57] J. K. A. P. P. e. a. Mills OH, "Comparing 2.5%, 5%, and 10% benzoyl peroxide on inflammatory acne vulgaris," 1986.

[58] N. C. Oprica C, "European surveillance study on the antibiotic susceptibility of Propionibacterium acnes." 2005.

[59] C. J. H. K. e. a. Eady EA, "Erythromycin resistant propionibacteria in antibiotic treated acne patients: association with treatment failure." 1989.

[60] A. W. Z. H. e. a. Worret I, "Acne resolution rates: results of a single-blind, randomized, controlled, parallel phase III trial with EE/CMA (Belara) and EE/LNG (Microgynon)." 2001.

[61] "ACOG practice bulletin no. 110: noncontraceptive uses of hormonal contraceptives." 2010.

[62] W. SE. "Comprehensive dermatologic drug therapy." 2007.

[63] D. C. Hull PR, "Isotretinoin use and subsequent depression and suicide." 2003.

[64] M. Kort, "inflammatory skin diseases treatment," skin disease and skin care, vol. 6, 2021.

[65] B. R. Hunt M. J, "A comparative study of gluconolactone versus benzoyl peroxide in the treatment of acne," 1992.

[66] H. C. U. R. McGuffin M, "Botanical Safety Handbook." 1997.

[67] B. M. R. "Alternative medicine and dermatology." 1998.

[68] H. G. Swords G, "Composition of Australian tea tree oil." 1978.

[69] F. P. S. E. Peirce A, "The American Pharmaceutical Association Practical Guide to Natural Medicines," 1999.

[70] R. J. H. M. Hausen B. M, "Degradation products of monoterpenes aresensitizing agents in tea tree oil." 1999.

[71] F. T. "Medical Economics Co.; PDR for Herbal Medicines." 2000.

[72] A. K. Yarnell E, "Herbal medicine for acne vulgaris." 2006.

[73] G. J. H. T. R. R. Blumenthal M, "The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicine," 1998.

[74] W. M. Bisset N. G, "Herbal Drugs and Phytopharmaceuticals." 2001.

[75] S. T. M. I. P. H. H. Lyss G, "an anti-inflammatory sesquiterpene lactone from arnica, selectively inhibits transcription factor NF-κB." 1997.

[76] 77D. A. Brown D. J, "Phytotherapeutic approaches to common dermatological conditions." 1998.

[77] S. M. R. M. H. A. W. B. G. G. Atherton D. J, "Treatment of atopic eczema with traditional Chinese medicinal plants." 1992.

[78] A. D. Sheehan M. P, "A controlled trial of traditional Chinese medicinal plants in widespread non-exudative atopic eczema." 1992.

[79] G.-B. R. "Toxicity of Chinese herbal remedies," 1992.

[80] W. B. R. M. A. D. B. J. Latchman Y, "The efficacy of traditional Chinese herbal therapy in atopic eczema." 1994.

[81] L. P. C. L. B. P. W. E. Fung A. Y, "A controlled trial of traditional Chinese herbal medicine in Chinese patients with recalcitrant atopic dermatitis." 1999.

[82] H. K. L. P. e. a. Chan B. C, "Traditional Chinese medicine for atopic eczema:PentaHerbs formula suppresses inflammatory mediators release from mast cells." 2008.

[83] L. H. K. S. e. a. Kim E. C, "The bark of Betula platyphylla var. japonica inhibits the developmentof atopic dermatitis-like skin lesions in NC/Nga mice." 2008.

[84] L. R. A. "Comparison of jewelweed and steroid in the treatment of poison ivy contact dermatitis." 1958.

[85] R. R. Guin J. D, "Jewelweed treatment of poison ivy dermatitis." 1980.

[86] B. N. M. J. J. Long D, "Treatment of poison ivy/oak allergic contact dermatitis with an extract of jewelweed." 1997.

[87] S.-K. M. H. H. L. P. S. M. Korting H. C, "Anti-inflammatory activity of hamamelis distillate applied topically to the skin." 1993.

[88] D. S. L. J. A. Ledezma E, "Efficacy of ajoene, an organosulphur derived from garlic, in the short-term therapy of tinea pedis." 1996.

[89] B. M. F. "Bacteriostatic activity of some Australian essential oils." 1979.

[90] A. P. B. R. Tong M. M, "Tea tree oil in the treatment of tinea pedis." 1992.

[91] N. D. A. J. Buck D. S, "Comparison of two topical preparations for the treatment of onychomycosis: Melaleuca alternifolia (tea tree) oil and clotrimazole." 1994.

[92] G. N. L. J. Faoagali J, "Does tea tree oil have a place in the topical treatment of burns?," 1997.

[93] S. I. "Antifungal activity of the extracts from Galla rhois against Candida albicans." 2007.

[94] A. S. H. A. A. S. A. S. A. M. Syed T. A, "Management of psoriais with aloe vera extract in a hydrophilic cream: A placebo-controlled, double-blind study." 1996.

[95] P. L. R. M. e. a. Bernstein J. E, "Effects of topically applied capsaicin on moderate and severe psoriasis vulgaris." 1986.

[96] B. B. S. V. e. a. Ellis C. N, "A double-blind evaluation of topical capsaicin in pruritic psoriasis." 1993.

[97] F. S. R. S. R. D. E. M. C. A. Fleischer A. B, "Alternative therapies commonly used within a population of patients with psoriasis," 1996.

[98] J. P. "Use of alternative medicine by patients with atopic dermatitis and psoriasis." 1990.

[99] N. S. K. "Topical traditional Chinese medicine." 1998.

[100] G. J. Zhang H, "Progress of experimental study on treatment of psoriasis by Chinese medicinal monomer and single or compound recipe in Chinese material medica." 2007.

[101] C. T. P. "Uses of turmeric in dentistry," 2009.

[102] S. M. H. J. H. M. Heng M. C, "Drug-induces suppression of phosphorylase kinase activity correlates with resolution of psoriasis as assessed by clinical, histological and immunohistochemical parameters." 2000.

[103] P. K. T. Y. Aziz H. A, "Solubility of core materials in aqueous polymeric solution effect on microencapsulation of curcumin." 2007.

[104] M. Z. Ahmad, "Nanoscale Topical Pharmacotherapy in Management of Psoriasis: Contemporary Research and Scope," MPDI, 2023.

[105] P. Negi, "Thymoquinone-loaded lipid vesicles: a promising nanomedicine for psoriasis," NIH, 2019.

[106] F. Shad, "The role of thymoquinone, a major constituent of Nigella sativa, in the treatment of inflammatory and infectious diseases." 2021.

[107] A. M. Yousuf, "Thymoquinone in autoimmune diseases: Therapeutic potential and molecular mechanisms," Biomedicine and Pharmacotherapy, 2021.

[108] A. Kmail, "How Thymoquinone from Nigella sativa Accelerates Wound Healing through Multiple Mechanisms and Targets," MPDI, 2023.

[109] E. Niculet, "Influence of phytochemicals in induced psoriasis (Review)," NCBI, 2020.

[110] K. Reich, "The concept of psoriasis as a systemic inflammation: implications for disease management," JEADV, 2012.

[111] R. Saraceno, "A European perspective on the challenges of managing psoriasis," PUB MED, 2006.

[112] S. R. Feldman, "The Challenge of Managing Psoriasis: Unmet Medical Needs and Stakeholder Perspectives," PUB MED, 2016.

[113] C. REID, "Psoriasis and Treatment: Past, Present and Future Aspects," PUB MED, 2020.

[114] A. Reich, "Speed of clinical improvement in the real-world setting from patient-reported Psoriasis Symptoms and Signs Diary: Secondary outcomes from the Psoriasis Study of Health Outcomes through 12weeks," JEADV, 2023.

[115] U. Mrowietz, "Psoriasis: to treat or to manage?," wiley online library, 2014.

[116] P. Rider, "Biologics for Targeting Inflammatory Cytokines, Clinical Uses, and Limitations," international journal of cell biology, 2016.

[117] K. F. Shad, "The role of thymoquinone, a major constituent of Nigella sativa, in the treatment of inflammatory and infectious diseases," Clinical and Experimental Pharmacology and Physiology, 2021.

[118] H. Shaterzadeh-Yazdi, "Immunomodulatory and Anti-inflammatory Effects of Thymoquinone," NIH, 2018.

[119] Y.-J. Surh, "Cancer chemoprevention with dietary phytochemicals," PUB MED, 2003.

[120] M. Y. Shahani, "Effect of Nigella sativa extract oil on granulation tissue in cutaneous wound: An experimental study in a rabbit model," Research gate, 2013.

[121] M. R. A. Rahman, "Evaluation of Wound Closure Activity of Nigella sativa, Melastoma malabathricum, Pluchea indica, and Piper sarmentosum Extracts on Scratched Monolayer of Human Gingival Fibroblasts," Evidence-Based Complementary and Alternative Medicine, 2014.

[122] y. liu, "The Role of Thymoquinone in Inflammatory Response in Chronic Diseases," 2022.

[123] S. C. McNeill, "Local Enhanced Topical Delivery (LETD) of Drugs: Does It Truly Exist?," springer link, vol. 9, 1992.

[124] A. Kaur, "Nanoemulsion loaded gel for topical co-delivery of clobitasol propionate and calcipotriol in psoriasis," pub med, 2017.

[125] M. Pradhan, "Novel colloidal carriers for psoriasis: current issues, mechanistic insight and novel delivery approaches," pub med, 2013.

[126] K. Mohsin, "Design of Lipid-Based Formulations for Oral Administration of Poorly Water-Soluble Drug Fenofibrate: Effects of Digestion," PUB MED, 2012.

[127] C. E. Umeyor, "Formulation of gentamicin as surface modified self-nanoemulsifying formulations (SNEFs) improves its anti-pneumococcal activity," European Journal of Nanomedicine, 2016.

[128] M. Alwadei, "Novel oral dosage regimen based on self-nanoemulsifying drug delivery systems for codelivery of phytochemicals – Curcumin and thymoquinone," Saudi Pharmaceutical Journal, vol. 27, no. 6, 2019.

[129] K. Khatoon, "Novel nanoemulsion gel containing triple natural bio-actives combination of curcumin, thymoquinone, and resveratrol improves psoriasis therapy: in vitro and in vivo studies," 2020.

[130] W. J. De Groot A. C, "Contact allergy to tea tree oil. Contact Dermatitis." 1993.

[131] E. C. "Tea tree oil poisoning." 1993.

[132] F. Zangeneh, "Psoriasis — Types, Causes and Medication," 2013.

[133] N. Michael Traub, "Psoriasis – Pathophysiology, Conventional, and Alternative Approaches to Treatment," 2007.

[134] P. Zhang, "The roles of T cells in psoriasis," 2023.

[135] X. J, "Advances in the Application of Natural Products and the Novel Drug Delivery Systems for Psoriasis." europe pmc, 2021.

[136] C. Blome, "Patient-relevant treatment goals in psoriasis," research gate, 2016.

[137] J. C. D. Res. "A study of clinical profile and quality of life in patients with scabies at a rural tertiary care Centre," 2016.

[138] K. C, "Global skin disease morbidity and mortality: an update from the global burden of disease study 2013," 2017.

[139] F. A. Wagener, "Targeting the redox balance in inflammatory skin conditions," 2013.

[140] Gupta, L., & Aggarwal, A. (2017). Inflammation in Psoriasis and Psoriatic Arthritis. In Psoriasis and Psoriatic Arthritis (pp. 35-44). CRC Press.

[141] A. Ragheb, "The Protective Effect of Thymoquinone, an Anti-Oxidant and Anti-Inflammatory Agent, Against Renal Injury," *saudi journal of kidney disease and transplantation,* 2009.

[142] S. Darakhshan, "Thymoquinone and its therapeutic potentials," *science direct,* 2015.

[143] H. Shaterzadeh-Yazdi, "Immunomodulatory and Anti-inflammatory Effects of Thymoquinone," *NIH,* 2018.

[144] Z. Kohandel, "Anti-inflammatory effects of thymoquinone and its protective effects against several diseases," *science direct,* 2021.

[145] A. B. Mehta, "Topical corticosteroids in dermatology," *indian journal of dermatology, venereology and leprology,* 2016.

Biography

Faizan Hamid, a dedicated medical professional, completed his MBBS from HITECH, Pakistan and is a registered medical practitioner with Pakistan. Furthermore, he holds registration with the General Medical Council (GMC) in the United Kingdom, solidifying his expertise as a doctor. Currently serving as a medical officer, Faizan is actively engaged in advancing healthcare and combating diseases. His current research endeavors are focused on the development and characterization of thymoquinone and hydrocortisone cream to address inflammatory skin conditions effectively. Through this research, Faizan aims to unlock the therapeutic potential of these compounds for patients grappling with various skin ailments, particularly focusing on alleviating the burdens of conditions like psoriasis. Faizan Hamid's commitment to enhancing healthcare and his specialized research in dermatology showcase his passion for making a tangible difference in the lives of those suffering from skin disorders.

Ayesha Hamid is a dedicated pharmacist who completed her Doctor of Pharmacy degree from the University of Central Punjab, Lahore, Pakistan. She is currently pursuing an MPhil in Pharmacology at Punjab University, where she continues to expand her expertise in the field of pharmacological sciences. Ayesha's professional journey as a pharmacist is marked by her commitment to advancing healthcare through research and innovation. Her current research focuses on the development and characterization of a thymoquinone and hydrocortisone cream for treating inflammatory skin conditions. Through this work, she aims to explore the therapeutic potential of these compounds and contribute to the field of dermatological treatments. Ayesha's academic achievements and professional experience reflect her passion for improving patient care and her dedication to finding innovative solutions to health challenges.